

Set	Items	Description
S1	8	CANCER-ASSOCIATED PROTEIN
S2	4	RD (unique items)
S3	0	ABOUT 28KD
S4	313	28KD
S5	90	S4 AND CANCER
S6	15	S5 AND BREAST
S7	15	RD (unique items)
?		

DIALOG on 1/17/2003

## Welcome to DialogClassic Web(tm)

Dialog level 02.12.20D  
Last logoff: 14jan03 10:04:44  
Logon file405 17jan03 08:39:37

## \*\*\* ANNOUNCEMENT \*\*\*

\*\*\*

--File 515 D&B Dun's Electronic Business Directory is now online completely updated and redesigned. For details, see HELP NEWS 515.

\*\*\*

--File 990 - NewsRoom now contains October 2002 to present records.  
File 993 - NewsRoom archive contains 2002 records from January 2002-September 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002

\*\*\*

--Alerts have been enhanced to allow a single Alert profile to be stored and run against multiple files. Duplicate removal is available across files and for up to 12 months. The Alert may be run according to the file's update frequency or according to a custom calendar-based schedule. There are no additional prices for these enhanced features. See HELP ALERT for more information.

\*\*\*

--U.S. Patents Fulltext (File 654) has been redesigned with new search and display features. See HELP NEWS 654 for information.

\*\*\*

--Connect Time joins DialUnits as pricing options on Dialog. See HELP CONNECT for information.

\*\*\*

--CLAIMS/US Patents (Files 340,341, 942) have been enhanced with both application and grant publication level in a single record. See HELP NEWS 340 for information.

\*\*\*

--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.

\*\*\*

--Important news for public and academic libraries. See HELP LIBRARY for more information.

\*\*\*

--Important Notice to Freelance Authors--  
See HELP FREELANCE for more information

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For information about the access to file 43 please see Help News43.

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## NEW FILES RELEASED

\*\*\*Dialog NewsRoom - Current 3-4 months (File 990)  
\*\*\*Dialog NewsRoom - 2002 Archive (File 993)  
\*\*\*Dialog NewsRoom - 2001 Archive (File 994)  
\*\*\*Dialog NewsRoom - 2000 Archive (File 995)  
\*\*\*TRADEMARKSCAN-Finland (File 679)  
\*\*\*TRADEMARKSCAN-Norway (File 678)  
\*\*\*TRADEMARKSCAN-Sweden (File 675)

\*\*\*

## UPDATING RESUMED

\*\*\*Delphes European Business (File 481)

\*\*\*

## RELOADED

\*\*\*D&B Dun's Electronic Business Directory (File 515)  
\*\*\*U.S. Patents Fulltext 1976-current (File 654)  
\*\*\*Population Demographics (File 581)  
\*\*\*Kompass Western Europe (File 590)  
\*\*\*D&B - Dun's Market Identifiers (File 516)

## REMOVED

\*\*\*Chicago Tribune (File 632)  
\*\*\*Fort Lauderdale Sun Sentinel (File 497)  
\*\*\*The Orlando Sentinel (File 705)

\*\*\*Newport News Daily Press (File 747)  
 \*\*\*U.S. Patents Fulltext 1980-1989 (File 653)  
 \*\*\*Washington Post (File 146)  
 \*\*\*Books in Print (File 470)  
 \*\*\*Court Filings (File 793)  
 \*\*\*Publishers, Distributors & Wholesalers of the U.S. (File 450)  
 \*\*\*State Tax Today (File 791)  
 \*\*\*Tax Notes Today (File 790)  
 \*\*\*Worldwide Tax Daily (File 792)

\*\*\* DIALOG HOMEBASE(SM) Main Menu \*\*\*

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. Data Star(R)

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/H = Help

/L = Logoff

/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

?

B PICKS

```

>>>          351 is unauthorized
>>>          352 is unauthorized
>>>2 of the specified files are not available
      17jan03 08:39:54 User243038 Session D111.1
      $0.00    0.225 DialUnits FileHomeBase
      $0.00 Estimated cost FileHomeBase
      $0.05 INTERNET
      $0.05 Estimated cost this search
      $0.05 Estimated total session cost    0.225 DialUnits
  
```

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2003/Jan W2  
(c) 2003 BIOSIS

**\*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.**

File 55:Biosis Previews(R) 1993-2003/Jan W2  
(c) 2003 BIOSIS

**\*File 55: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.**

File 159:Cancerlit 1975-2002/Oct  
(c) format only 2002 Dialog Corporation

File 143:Biol. & Agric. Index 1983-2003/Dec  
(c) 2003 The HW Wilson Co

File 358:Current BioTech Abs 1983-2002/Dec  
(c) 2002 DECHEMA

File 340:CLAIMS(R)/US Patent 1950-03/Jan 14  
(c) 2003 IFI/CLAIMS(R)

**\*File 340: Application & grant publications are in 1 record. See HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.**

File 344:Chinese Patents Abs Aug 1985-2002/Nov  
(c) 2002 European Patent Office

File 348:EUROPEAN PATENTS 1978-2003/Jan W02

(c) 2003 European Patent Office  
 File 447:IMS Patent Focus 2002/Dec  
 (c) 2002 IMS Health & Affiliates  
 File 72:EMBASE 1993-2003/Jan W2  
 (c) 2003 Elsevier Science B.V.  
**\*File 72: Alert feature enhanced for multiple files, duplicates**  
 removal, customized scheduling. See HELP ALERT.  
 File 73:EMBASE 1974-2003/Jan W2  
 (c) 2003 Elsevier Science B.V.  
**\*File 73: Alert feature enhanced for multiple files, duplicates**  
 removal, customized scheduling. See HELP ALERT.  
 File 154:MEDLINE(R) 1990-2003/Jan W1  
**\*File 154: Updating of completed records has resumed.** See Help News154.  
 Alert feature enhanced with customized scheduling. See HELP ALERT.  
 File 155:MEDLINE(R) 1966-2003/Jan W1  
**\*File 155: Updating of completed records has resumed.** See Help News155.  
 Alert feature enhanced with customized scheduling. See HELP ALERT.  
 File 349:PCT FULLTEXT 1979-2002/UB=20030116,UT=20030109  
 (c) 2003 WIPO/Univentio

Set	Items	Description
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S CANCER-ASSOCIATED PROTEIN

S1 8 CANCER-ASSOCIATED PROTEIN

?

RD

&gt;&gt;&gt;Duplicate detection is not supported for File 340.

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&gt;&gt;&gt;Duplicate detection is not supported for File 348.

&gt;&gt;&gt;Duplicate detection is not supported for File 447.

&gt;&gt;&gt;Duplicate detection is not supported for File 349.

&gt;&gt;&gt;Records from unsupported files will be retained in the RD set.

...completed examining records

S2 4 RD (unique items)

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T S4/5/ALL

&gt;&gt;&gt;Set 4 does not exist

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T S2/5/ALL

2/5/1 (Item 1 from file: 5)

DIALOG(R)File 5:BIOSIS Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

13828895 BIOSIS NO.: 200200457716

**Interactions of the NaPi cotransporter IIa in the brush border of proximal tubular cells.**

AUTHOR: Deliot Nadine(a); Gisler Serge(a); Pribanic Sandra(a); Hernando Nati(a); Biber Jurg(a); Murer Heini(a)

AUTHOR ADDRESS: (a)Institute of Physiology, University Zurich, Zurich\*\* Switzerland

JOURNAL: Journal of General Physiology 120 (1):p8a-9a July, 2002

MEDIUM: print

CONFERENCE/MEETING: Fifty-sixth Annual Meeting of the Society of General Physiologists Woods Hole, MA, USA September 04-08, 2002

ISSN: 0022-1295

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology; Urinary System (Chemical Coordination and Homeostasis)

ORGANISMS: PARTS ETC: proximal tubular cells--brush border, excretory system

CHEMICALS & BIOCHEMICALS: MAP17--**cancer-associated protein** ; VILIP-3  
--calcium-binding protein; sodium phosphate-cotransporter IIa  
MISCELLANEOUS TERMS: endocytosis; Meeting Abstract; Meeting Poster  
CONCEPT CODES:

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals  
02502 Cytology and Cytochemistry-General  
02506 Cytology and Cytochemistry-Animal  
10060 Biochemical Studies-General  
15504 Urinary System and External Secretions-Physiology and  
Biochemistry

2/5/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

13780594 BIOSIS NO.: 200200409415

**Identification of diubiquitin as a cancer-associated protein.**

AUTHOR: Ren Jianwei(a); Cheong Ian; Jin Rongxian; Ban Kenneth; Ooi London  
Lucien; Nuchprayoon Issarang; Lee Kang Hoe; Choti Michael; Dang Chi V;  
Lee Linda A; Lee Caroline G

AUTHOR ADDRESS: (a)Johns Hopkins Singapore, Singapore\*\*Singapore

JOURNAL: Proceedings of the American Association for Cancer Research Annual  
Meeting 43p819 March, 2002

MEDIUM: print

CONFERENCE/MEETING: 93rd Annual Meeting of the American Association for  
Cancer Research San Francisco, California, USA April 06-10, 2002

ISSN: 0197-016X

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Digestive System  
(Ingestion and Assimilation); Tumor Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,  
Animalia

ORGANISMS: human (Hominidae)--female

ORGANISMS: PARTS ETC: gastrointestinal tract--digestive system; liver--  
digestive system; uterus--reproductive system

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans;  
Mammals; Primates; Vertebrates

DISEASES: colorectal cancer--digestive system disease, etiology,  
neoplastic disease; hepatocellular carcinoma--digestive system disease  
, etiology, neoplastic disease; uterine cancer--neoplastic disease,  
reproductive system disease/female

CHEMICALS & BIOCHEMICALS: MAD2; diubiquitin--**cancer-associated  
protein**, regulation

MISCELLANEOUS TERMS: cDNA microarray {complementary DNA microarray};  
Meeting Abstract

ALTERNATE INDEXING: Colorectal Neoplasms (MeSH); Carcinoma, Hepatocellular  
(MeSH); Uterine Neoplasms (MeSH)

CONCEPT CODES:

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals  
10060 Biochemical Studies-General  
14004 Digestive System-Physiology and Biochemistry  
14006 Digestive System-Pathology  
16504 Reproductive System-Physiology and Biochemistry  
16506 Reproductive System-Pathology  
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects;  
Systemic Effects

BIOSYSTEMATIC CODES:

86215 Hominidae

2/5/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

12304759 BIOSIS NO.: 200000062626

**Structural studies of tNOX periodicity.**

AUTHOR: Myers Rebecca(a); Kelker Matthew(a); Kim Chinpal(a); Chueh Pinju(a)  
; Morre Dorothy M(a); Morre D James(a)

AUTHOR ADDRESS: (a)Purdue University, West Lafayette, IN\*\*USA

JOURNAL: Molecular Biology of the Cell 10 (SUPPL.):p210a Nov., 1999

CONFERENCE/MEETING: 39th Annual Meeting of the American Society for Cell  
Biology Washington, D.C., USA December 11-15, 1999

SPONSOR: The American Society for Cell Biology

ISSN: 1059-1524

RECORD TYPE: Citation

LANGUAGE: English

**DESCRIPTORS:**

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell  
Biology); Tumor Biology

BIOSYSTEMATIC NAMES: Animalia

ORGANISMS: animal (Animalia)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals

CHEMICALS & BIOCHEMICALS: membrane proteins--function, structure; tNOX  
--alpha-helix-beta-sheet transformation,**cancer-associated protein** ,  
cloned, constitutive form, expression, hydroquinone oxidase,  
periodicity, protein disulfide-thiol interchange activity, structure,  
temperature effect

MISCELLANEOUS TERMS: Meeting Abstract

**CONCEPT CODES:**

02506 Cytology and Cytochemistry-Animal

07200 Circadian Rhythms and Other Periodic Cycles

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

10802 Enzymes-General and Comparative Studies; Coenzymes

24006 Neoplasms and Neoplastic Agents-Biochemistry

23001 Temperature: Its Measurement, Effects and Regulation-General  
Measurement and Methods

10502 Biophysics-General Biophysical Studies

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals

**BIOSYSTEMATIC CODES:**

33000 Animalia-Unspecified

2/5/4 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

12304758 BIOSIS NO.: 200000062625

**Function of tNOX, a cancer-associated protein, in cell enlargement.**

AUTHOR: Chueh Pinju(a); Tang Xiaoyu(a); Wu Lian-Ying(a); Morre Dorothy M(a)  
; Morre D James(a)

AUTHOR ADDRESS: (a)Purdue University, West Lafayette, IN\*\*USA

JOURNAL: Molecular Biology of the Cell 10 (SUPPL.):p209a Nov., 1999

CONFERENCE/MEETING: 39th Annual Meeting of the American Society for Cell  
Biology Washington, D.C., USA December 11-15, 1999

SPONSOR: The American Society for Cell Biology

ISSN: 1059-1524

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 404-86-4: CAPSAICIN; 989-51-5: EPIGALLOCATECHIN GALLATE

**DESCRIPTORS:**

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell  
Biology); Tumor Biology

BIOSYSTEMATIC NAMES: Cercopithecidae--Primates, Mammalia, Vertebrata,  
Chordata, Animalia

ORGANISMS: COS cell line (Cercopithecidae)  
 BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals;  
 Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates;  
 Vertebrates  
 CHEMICALS & BIOCHEMICALS: capsaicin--enzyme inhibitor;  
 epigallocatechin gallate--enzyme inhibitor; membrane proteins--  
 function, structure; tNOX--**cancer-associated protein**, hydroquinone  
 oxidase, protein disulfide-thiol interchange activity; tNOX cDNA {tNOX  
 complementary DNA  
 MISCELLANEOUS TERMS: cell enlargement; Meeting Abstract  
 CONCEPT CODES:  
 02506 Cytology and Cytochemistry-Animal  
 10064 Biochemical Studies-Proteins, Peptides and Amino Acids  
 10502 Biophysics-General Biophysical Studies  
 22002 Pharmacology-General  
 24006 Neoplasms and Neoplastic Agents-Biochemistry  
 10802 Enzymes-General and Comparative Studies; Coenzymes  
 00520 General Biology-Symposia, Transactions and Proceedings of  
 Conferences, Congresses, Review Annuals  
 BIOSYSTEMATIC CODES:  
 86205 Cercopithecidae  
 ?  
 S ABOUT 28KD  
 S3 0 ABOUT 28KD  
 ?  
 S 28KD  
 S4 313 28KD  
 ?  
 S S4 AND CANCER  
 313 S4  
 3264565 CANCER  
 S5 90 S4 AND CANCER  
 ?  
 S S5 AND BREAST  
 90 S5  
 852262 BREAST  
 S6 15 S5 AND BREAST  
 ?  
 RD  
 >>>Duplicate detection is not supported for File 340.  
 >>>Duplicate detection is not supported for File 344.  
 >>>Duplicate detection is not supported for File 348.  
 >>>Duplicate detection is not supported for File 447.  
 >>>Duplicate detection is not supported for File 349.  
 >>>Records from unsupported files will be retained in the RD set.  
 ...completed examining records  
 S7 15 RD (unique items)  
 ?  
 T S7/5/ALL  
 7/5/1 (Item 1 from file: 349)  
 DIALOG(R) File 349:PCT FULLTEXT  
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00970021

**METHODS OF DIAGNOSIS OF OVARIAN CANCER , COMPOSITIONS AND METHODS OF  
 SCREENING FOR MODULATORS OF OVARIAN CANCER  
 PROCEDES DE DIAGNOSTIC DU CANCER OVARIEN, COMPOSITIONS ET PROCEDES DE  
 CRIBLAGE DE MODULATEURS DU CANCER OVARIEN**

Patent Applicant/Assignee:

EOS BIOTECHNOLOGY INC, 225A Gateway Boulevard, South San Francisco, CA  
 94080, US, US (Residence), US (Nationality), (For all designated states  
 except: US)

Patent Applicant/Inventor:

MACK David H, 2076 Monterey Avenue, Menlo Park, CA 94025, US, US  
(Residence), US (Nationality), (Designated only for: US)  
GISH Kurt C, 40 Perego Terrace #2, San Francisco, CA 94131, US, US  
(Residence), US (Nationality), (Designated only for: US)

## Legal Representative:

BASTIAN Kevin L (et al) (agent), Townsend and Townsend and Crew LLP, Two  
Embarcadero Center, 8th Floor, San Francisco, CA 94111, US,

## Patent and Priority Information (Country, Number, Date):

Patent: WO 2002102235 A2 20021227 (WO 02102235)  
Application: WO 2002US19297 20020618 (PCT/WO US0219297)  
Priority Application: US 2001299234 20010618; US 2001315287 20010827; US  
2001317544 20010905; US 2001350666 20011113; US 2002372246 20020412

## Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO  
RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: A61B

Publication Language: English

Filing Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 223312

## English Abstract

Described herein are genes whose expression are up-regulated or  
down-regulated in ovarian**cancer** . Related methods and compositions that  
can be used for diagnosis and treatment of ovarian**cancer** are  
disclosed. Also described herein are methods that can be used to identify  
modulators of ovarian**cancer** .

## French Abstract

L'invention concerne des genes dont l'expression est regulee positivement  
ou negativement dans le**cancer** ovarien. Elle concerne egalement des  
procedes et des compositions qui peuvent etre utilises dans le diagnostic  
et le traitement du**cancer** ovarien, ainsi que des procedes  
d'identification de modulateurs du**cancer** ovarien.

## Legal Status (Type, Date, Text)

Publication 20021227 A2 Without international search report and to be  
republished upon receipt of that report.

7/5/2 (Item 2 from file: 349)

DIALOG(R) File 349: PCT FULLTEXT

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00962329

## MOLECULAR TOXICOLOGY MODELING

## MODELISATION EN TOXICOLOGIE MOLECULAIRE

Patent Applicant/Assignee:

GENE LOGIC INC, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:

MENDRICK Donna, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (Designated only for: US)

PORTER Mark, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (Designated only for: US)

JOHNSON Kory, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (Designated only for: US)

HIGGS Brandon, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US



(Residence), US (Nationality), (Designated only for: US)  
CASTLE Arthur, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (Designated only for: US)  
ELASHOFF Michael, 708 Quince Orchard Road, Gaithersburg, MD 20878, US, US  
(Residence), US (Nationality), (Designated only for: US)

## Legal Representative:

TUSCAN Michael S (et al) (agent), Morgan, Lewis & Bockius LLP, 1111  
Pennsylvania Avenue, NW, Washington, DC 20004, US,

## Patent and Priority Information (Country, Number, Date):

Patent: WO 200295000 A2 20021128 (WO 0295000)  
Application: WO 2002US16173 20020522 (PCT/WO US0216173)  
Priority Application: US 2001292335 20010522; US 2001297523 20010613; US  
2001298925 20010619; US 2001303807 20010710; US 2001303808 20010710; US  
2001303810 20010710; US 2001315047 20010828; US 2001324928 20010927; US  
2001330462 20011022; US 2001330867 20011101; US 2001331805 20011121; US  
2001336144 20011206; US 2001340873 20011219; US 2002357843 20020221; US  
2002357844 20020221; US 2002357842 20020221; US 2002364134 20020315; US  
2002370144 20020408; US 2002370206 20020408; US 2002370247 20020408; US  
2002372794 20020417; US 2002371679 20020421

## Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO  
RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW  
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR  
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: C12N

Publication Language: English

Filing Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 160203

## English Abstract

The present invention is based on the elucidation of the global changes in gene expression and the identification of toxicity markers in tissues or cells exposed to a known renal toxin. The genes may be used as toxicity markers in drug screening and toxicity assays. The invention includes a database of genes characterized by toxin-induced differential expression that is designed for use with microarrays and other solid-phase probes.

## French Abstract

L'invention est basee sur l'elucidation des changements globaux intervenant dans l'expression genique et l'identification des marqueurs de toxicite dans les tissus ou les cellules exposes a une toxine renale connue. Les genes peuvent etre utilises comme marqueurs de toxicite dans la selection des medicaments et les dosages de toxicite. L'invention comprend une base de donnees de genes caracterisee par l'expression differentielle provoquee par une toxine qui est prevue pour l'utilisation avec des micro-arrangements et autres sondes a phase solide.

## Legal Status (Type, Date, Text)

Publication 20021128 A2 Without international search report and to be republished upon receipt of that report.

Publication 20021128 A2 Sequence listing published separately in electronic form and available upon request from the International Bureau.

7/5/3 (Item 3 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00948768

HEDGEHOG

HEDGEHOG

## Patent Applicant/Assignee:

LORANTIS LIMITED, 307 Cambridge Science Park, Milton Road, Cambridge CB4  
0WG, GB, GB (Residence), GB (Nationality), (For all designated states  
except: US)

## Patent Applicant/Inventor:

LAMB Jonathan Robert, The University of Edinburgh Medical School, Teviot  
Place, Edinburgh EH8 9AG, GB, GB (Residence), GB (Nationality),  
(Designated only for: US)

HOYNE Gerard Francis, The University of Edinburgh Medical School, Teviot  
Place, Edinburgh EH8 9AG, GB, GB (Residence), AU (Nationality),  
(Designated only for: US)

DALLMAN Margaret Jane, Imperial College of Science Technology & Medicine,  
Imperial College Road, London SW7 2AZ, GB, GB (Residence), GB  
(Nationality), (Designated only for: US)

CHAMPION Brian Robert, Lorantis Limited, Babraham Hall, Babraham,  
Cambridge CB2 4UL, GB, GB (Residence), GB (Nationality), (Designated  
only for: US)

## Legal Representative:

MALLALIEU Catherine Louise (et al) (agent), D. Young & Co., 21 New Fetter  
Lane, London EC4A 1DA, GB,

## Patent and Priority Information (Country, Number, Date):

Patent: WO 200280952 A2 20021017 (WO 0280952)

Application: WO 2002GB1666 20020409 (PCT/WO GB0201666)

Priority Application: GB 20018872 20010409; GB 20018873 20010409

## Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO

RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: A61K-038/00

Publication Language: English

Filing Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 38140

English Abstract

Use of a modulator of a Hedgehog signalling pathway, or a modulator of a  
pathway which is a target of the Hedgehog signalling pathway in the  
preparation of a medicament for treatment of a disease or disorder  
associated with a T-cell mediated disease or disorder.

French Abstract

La presente invention concerne l'utilisation d'un modulateur de la voie  
de signalisation Hedgehog ou d'un modulateur d'une voie qui est la cible  
de la voie de signalisation Hedgehog, dans la preparation d'un medicament  
destine au traitement d'une maladie ou d'une affection associee a une  
maladie ou une affection mediee par les lymphocytes T.

Legal Status (Type, Date, Text)

Publication 20021017 A2 Without international search report and to be  
republished upon receipt of that report.

Examination 20021205 Request for preliminary examination prior to end of  
19th month from priority date

7/5/4 (Item 4 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00942411

**METHOD FOR THERAPEUTICALLY TREATING A CLINICALLY RECOGNIZED FORM OF  
CARDIOPATHOLOGY IN A LIVING MAMMAL**  
**METHODE DE TRAITEMENT THERAPEUTIQUE D'UNE FORME CLINIQUEMENT IDENTIFIEE DE  
CARDIOPATHIE CHEZ UN MAMMIFERE VIVANT**

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Patent and Priority Information (Country, Number, Date):

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Application: WO 2002US7555 20020314 (PCT/WO US0207555)

Priority Application: US 2001276148 20010315; US 2001276147 20010315; US  
2001276247 20010315; US 2001276246 20010315; US 2001276245 20010315; US  
2001276244 20010315; US 2001276243 20010315; US 2001276175 20010315

Designated States: AU CA JP US

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Main International Patent Class: G01N-033/00

International Patent Class: A01K-067/00; A01K-067/027; A01K-067/033;  
A01N-043/04; A01N-063/00; A61K-031/70; A61K-048/00; C12N-005/00;  
C12N-005/02

Publication Language: English

Filing Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 36307

**English Abstract**

The present invention provides therapeutic methods which employ one or more identifiable types of mammalian stem cells, and/or their progenitor progeny cells, and/or their lineage-committed descendant cells, and/or their partially-differentiated offspring cells - with or without completely differentiated cells to treat living mammalian subjects afflicted with a clinically recognized form of cardiopathology. The identifiable cell types include embryonic stem cells and their offspring cells; as well as the presently identified types of adult stem cells and their various offspring cells; and also include recently identified alternative cells types which have functional stem cell properties. Among the clinical forms of cardiopathology which can be efficaciously treated using the present therapeutic methods are myocardial infarction, myocarditis, heart failure, and cardiac dysrhythmia.

**French Abstract**

La presente invention concerne des methodes therapeutiques faisant appel a un ou plusieurs type(s) identifiable(s) de cellules souches mammaliennes et/ou de cellules progenitrices qui en sont issues, et/ou de cellules issues de leurs lignees, et/ou de cellules partiellement differenciees issues desdites cellules souches avec ou sans cellules totalement differenciees dans le but de traiter des mammiferes souffrant d'une forme de cardiopathie cliniquement identifiee. Les types de cellules identifiabiles comprennent des cellules souches embryonnaires et les cellules qui en sont issues, les types de cellules souches adultes actuellement identifiees et les differentes cellules qui en sont issues, ainsi que des types de cellules alternatives identifiees recemment et presentant des proprietes fonctionnelles de cellules souches. Parmi les formes cliniques de cardiopathies qui peuvent etre traitees efficacement au moyen des methodes therapeutiques selon la presente invention figurent

l'infarctus du myocarde, la myocardite, l'insuffisance cardiaque et la dysrythmie cardiaque.

Legal Status (Type, Date, Text)

Publication 20020926 A1 With international search report.

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00938026

METHODS, SYSTEMS AND COMPUTER PROGRAM PRODUCTS FOR DETERMINING THE BIOLOGICAL EFFECT AND/OR ACTIVITY OF DRUGS, CHEMICAL SUBSTANCES AND/OR PHARMACEUTICAL COMPOSITIONS BASED ON THEIR EFFECT ON THE METHYLATION STATUS OF THE DNA

PROCEDES, SYSTEMES ET PRODUITS PROGRAMMES INFORMATIQUES PERMETTANT DE DETERMINER L'EFFET BIOLOGIQUE ET/OU L'ACTIVITE DE MEDICAMENTS, DE SUBSTANCES CHIMIQUES ET/OU DE COMPOSITIONS PHARMACEUTIQUES, SUR LA BASE DE LEUR EFFET SUR L'ETAT DE METHYLATION DE L'ADN

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200270741 A2 20020912 (WO 0270741)

Application: WO 2002EP2254 20020301 (PCT/WO EP0202254)

Priority Application: US 2001272484 20010301

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CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO

RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: C12Q-001/68

Publication Language: English

Filing Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 40809

English Abstract

This invention is related to methods, systems and computer program products for determining the biological effect and/or activity of drugs, chemical substances and/or pharmaceutical compositions using their effect on DNA-methylation as a marker for their biological effect(s). The invention is further related to the use of the inventive methods, systems and computer program products in obtaining new biologically active compounds which can be used as so-called "lead" compounds for new and effective medicaments and treatment strategies of, in particular, human diseases.

French Abstract

La presente invention concerne des procedes, des systemes et des produits

programmes informatiques permettant de determiner l'effet biologique et/ou l'activite de medicaments, de substances chimiques et/ou de compositions pharmaceutiques, sur la base de leur effet sur la methylation de l'ADN, qui sert de marqueur pour leur(s) effet(s) biologique(s). La presente invention concerne egalement l'utilisation des procedes, des systemes et des produits programmes informatiques selon cette invention, afin d'obtenir de nouveaux composees biologiquement actifs, qui peuvent etre utilises en tant que <= tete de serie >= pour de nouveaux medicaments et de nouvelles strategies de traitement efficaces, notamment pour des maladies humaines.

Legal Status (Type, Date, Text)

Publication 20020912 A2 Without international search report and to be republished upon receipt of that report.

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7/5/6 (Item 6 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00878401 \*\*Image available\*\*

**IDENTIFYING DRUGS FOR AND DIAGNOSIS OF BENIGN PROSTATIC HYPERPLASIA USING GENE EXPRESSION PROFILES**

**IDENTIFICATION DE MEDICAMENTS CONTRE L'HYPERPLASIA PROSTATIQUE BENINE ET DIAGNOSTIC DE LADITE HYPERPLASIA AU MOYEN DE PROFILS D'EXPRESSION GENIQUE**

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200212440 A2-A3 20020214 (WO 0212440)  
Application: WO 2001US24708 20010807 (PCT/WO US0124708)  
Priority Application: US 2000223323 20000807; US 2001873319 20010605

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU  
CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD  
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR  
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW  
(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: C12Q-001/68

Publication Language: English  
Filing Language: English  
Fulltext Availability:  
Detailed Description  
Claims  
Fulltext Word Count: 26791

#### English Abstract

The present invention is based on the elucidation of the global changes in gene expression in prostate tissue isolated from patients exhibiting different clinical states of prostate hyperplasia as compared to normal prostate tissue as well as the identification of individual genes that are differentially expressed in diseased prostate tissue.

#### French Abstract

La presente invention est fondee sur l'elucidation des changements globaux d'expression genique dans un tissu prostatique isole de patients presentant differents etats cliniques d'hyperplasie prostatique, par rapport a un tissu prostatique normal. Cette invention concerne egalement l'identification de genes individuels differemment exprimes dans un tissu prostatique infecte.

#### Legal Status (Type, Date, Text)

Publication 20020214 A2 Without international search report and to be republished upon receipt of that report.  
Search Rpt 20021107 Late publication of international search report  
Republication 20021107 A3 With international search report.  
Examination 20021212 Request for preliminary examination prior to end of 19th month from priority date

7/5/7 (Item 7 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00833557 \*\*Image available\*\*

#### COUPLED TWO-WAY CLUSTERING ANALYSIS OF DATA

#### ANALYSE DE DONNEES PAR GROUPEMENT BIDIRECTIONNEL COUPLE

#### Patent Applicant/Assignee:

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#### Patent and Priority Information (Country, Number, Date):

Patent: WO 200167061 A2-A3 20010913 (WO 0167061)  
Application: WO 2001IL228 20010309 (PCT/WO IL0100228)  
Priority Application: IL 134994 20000309

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU  
CZ DE DE (utility model) DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ  
PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR  
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG  
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW  
(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: G06F-019/00

Publication Language: English

Filing Language: English  
Fulltext Availability:  
Detailed Description  
Claims  
Fulltext Word Count: 28249

#### English Abstract

A novel coupled two-way clustering approach to gene microarray data analysis, for identifying subsets of the genes and samples, such that when one of these items is used to cluster the other, stable and significant partitions emerge. The method of the present invention preferably uses iterative clustering in order to execute this search in an efficient way. This approach is especially suitable for gene microarray data, where the contributions of a variety of biological mechanisms to the gene expression levels are entangled in a large body of experimental data. The method of the present invention was applied to two gene microarray data sets, on coloncancer and leukemia. By identifying relevant subsets of the data and focusing on these subsets, partitions and correlations were found that were masked and hidden when the full data set was used in the analysis.

#### French Abstract

L'invention concerne une nouvelle approche de groupement bidirectionnel couple concernant l'analyse de donnees relatives a un jeu ordonne de microechantillons geniques, qui permet d'identifier des sous-ensembles des genes et echantillons, si bien que, lorsqu'un de ces articles est utilise pour agglomerer l'autre, on cree des separations stables et significatifs. Le procede de l'invention met en oeuvre, de preference, un groupement iteratif pouvant executer cette recherche de maniere efficace. Cette approche convient particulierement pour des donnees relatives a un jeu ordonne de microechantillons geniques dans lequel les apports de divers mecanismes biologiques aux niveaux de l'expression genique sont enchevetres dans un grand corps de donnees experimentales. Le procede de l'invention a ete applique a deux ensembles de donnees relatives a un jeu ordonne de microechantillons geniques concernant le cancer du colon et la leucemie. En identifiant des sous-ensembles pertinents des donnees et en se focalisant sur ces sous-ensembles, l'on a decouvert des separations et des correlations qui etaient masquees ou cachees quand l'ensemble de donnees au complet etait utilise pour effectuer l'analyse.

#### Legal Status (Type, Date, Text)

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Search Rpt 20020404 Late publication of international search report  
Republication 20020404 A3 With international search report.  
Examination 20030103 Request for preliminary examination prior to end of 19th month from priority date

7/5/8 (Item 8 from file: 349)  
DIALOG(R) File 349: PCT FULLTEXT  
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00577376 \*\*Image available\*\*

**METHOD FOR THE DETECTION OF GENE TRANSCRIPTS IN BLOOD AND USES THEREOF**  
**TECHNIQUE DE DETECTION DE TRANSCRITS GENIQUES DANS LE SANG ET LEUR**  
**UTILISATION**

Patent Applicant/Assignee:

LIEW Choong-Chin,

Inventor(s):

LIEW Choong-Chin,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200040749 A2 20000713 (WO 0040749)

Application: WO 2000CA5 20000105 (PCT/WO CA00000005)

Priority Application: US 99115125 19990106; US 2000477148 20000104

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK  
 DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
 LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ  
 TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM  
 AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL  
 PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

Main International Patent Class: C12Q-001/68

Publication Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 24255

#### English Abstract

The present invention is directed to detection and measurement of gene transcripts in blood. Specifically provided is a RT-PCR analysis performed on a drop of blood for detecting, diagnosing and monitoring diseases using tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-associated genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

#### French Abstract

Cette invention a trait a la detection et a la mesure de transcrits geniques dans du sang. Elle concerne plus precisement une analyse PCR-ADNC effectuee sur une goutte de sang aux fins de la detection, du diagnostic et de la surveillance de maladies a l'aide d'amorces a specificite tissulaire. Elle porte egalement sur des techniques par le moyen desquelles la delimitation de la sequence et/ou la quantification des taux d'expression de genes associes a des maladies permet(tent) d'effectuer un essai de diagnostic/pronostic immediat et precis relatif a une maladie ou permet(tent) d'evaluer l'effet d'un schema particulier de traitement.

7/5/9 (Item 9 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00543665

#### PROTEIN FRAGMENT COMPLEMENTATION ASSAYS

DOSAGES DE COMPLEMENTATION PROTEINES-FRAGMENTS POUR LA DETECTION  
 D'INTERACTIONS BIOLOGIQUES OU ENTRE MEDICAMENTS

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200007038 A2 20000210 (WO 0007038)

Application: WO 99CA702 19990730 (PCT/WO CA9900702)

Priority Application: CA 2244349 19980730; US 98124850 19980730

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT  
 LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT  
 UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD  
 RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF  
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International Patent Class: G01N-033/566; G01N-033/68



Publication Language: English  
Fulltext Availability:  
Detailed Description  
Claims  
Fulltext Word Count: 28092

#### English Abstract

A Protein Complementation Assay/Universal Reporter System (PCA/URS) for detecting and screening for agonists and antagonists of a cellular receptor is described. The invention is illustrated by the example of murine dihydrofolate reductase (DHFR). Fusion peptides consisting of N- and C terminal fragments of murine DHFR fused to GCN4 leucine zipper sequences were coexpressed in *Escherichia coli* grown in minimal medium, where the endogenous DHFR activity was inhibited with trimethoprim. Coexpression of the complementary fusion products restored colony formation. Survival only occurred when both DHFR fragments were present and contained leucine-zipper forming sequences, demonstrating that reconstitution of enzyme activity requires assistance of leucine zipper formation. This assay could be used to study equilibrium and kinetic aspects of various molecular interactions.

#### French Abstract

Cette invention se rapporte a une strategie permettant de concevoir et de mettre en oeuvre des dosages de complementation proteines-fragments (PCA), afin de detecter les interactions biomoleculaires *i*(in vivo) et *i*(in vitro). Un systeme de reporteur universel/dosage de complementation de proteines (PCA/URS), servant a detecter et a cribler des agonistes et des antagonistes d'un recepteur de membranes, est egalement presente. La conception, la mise en oeuvre et les vastes applications de cette strategie sont illustrees par un grand nombre d'enzymes, avec des details particuliers fournis pour l'exemple de la dihydrofolate reductase (DHFR) murine. Des peptides de fusion, constitues par le fragment N-terminal et le fragment C-terminal de l'enzyme DHFR murine, fusionnes avec des sequences glissieres de leucine GCN4, ont ete coexprimes dans l'*i*(*Escherichia coli*) cultive dans un milieu minimal, dans lequel l'activite DHFR endogene a ete inhibee par la trimethoprim. La coexpression de ces produits de fusion complementaires a retabli la formation de colonies. La survie n'a pu etre observee que lorsque les deux fragments de DHFR etaient presents et contenaient des sequences de formation de glissieres de leucine, montrant ainsi que le retablisement de l'activite enzymatique necessite l'assistance de la formation de glissieres de leucines. Des mutants a points d'interface entre fragments DHFR, d'une severite croissante (Ile a Val, Ala et Gly) ont entraines une augmentation sequentielle des temps de doublage de l'*i*(*E. coli*), illustrant ainsi le reassemblage reussi des fragments de DHFR, plutot que les interactions non specifiques entre les fragments. Ce dosage pourrait etre utilise pour etudier l'equilibre et les aspects cinetiques des interactions moleculaires, y compris divers types d'interactions. Les criteres de selection et de conception appliques ici sont developpes pour de nombreux exemples de selection de clones, colorimetrique, fluorometrique et autres dosages bases sur des enzymes dont les produits peuvent etre mesures. Le developpement de ces systemes de dosages s'est revele simple et permet une grande variete d'applications de complementation proteines-fragments.

7/5/10 (Item 10 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00462134

**NOVEL ADMINISTRATION OF THROMBOPOIETIN**  
**NOUVEAU PROCEDE D'ADMINISTRATION DE THROMBOPOIETINE**  
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## Patent and Priority Information (Country, Number, Date):

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Application: WO 98US10475 19980521 (PCT/WO US9810475)  
Priority Application: US 97859767 19970521; US 9815016 19980128

Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES  
FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD  
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US  
UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE  
CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN  
ML MR NE SN TD TG

Main International Patent Class: A61K-038/19

International Patent Class: A61K-35:14

Publication Language: English

Fulltext Availability:

Detailed Description  
Claims

Fulltext Word Count: 30294

## English Abstract

Thrombopoietin materials can be administered with substantial therapeutic effect in a single or low-multiple daily administration. Reversal of thrombocytopenia is achieved by administering to a patient having or in need of such treatment a single or low-multiple daily dose of a therapeutically effective amount of a thrombopoietin.

## French Abstract

L'invention concerne des matieres de thrombopoietine pouvant etre administrees de facon a obtenir un effet sensiblement therapeutique en une seule prise quotidienne ou en plusieurs prises a faible dose. On obtient une inversion de la thrombocytopenie en administrant a un patient atteint de cette maladie ou necessitant un tel traitement une seule dose quotidienne ou de multiples faibles doses d'une quantite therapeutiquement efficace d'une thrombopoietine.

7/5/11 (Item 11 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00424010

**PFS28 FUSION PROTEINS**

**PROTEINES DE FUSION PFS28**

Patent Applicant/Assignee:

THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by THE  
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GOZAR Mary Margaret,

Inventor(s):

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GOZAR Mary Margaret,  
Patent and Priority Information (Country, Number, Date):  
Patent: WO 9814472 A1 19980409  
Application: WO 97US17666 19970929 (PCT/WO US9717666)  
Priority Application: US 9627390 19960930  
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES  
FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK  
MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN  
YU ZW GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK  
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN  
TD TG  
Main International Patent Class: C07K-014/445  
International Patent Class: C12N-15:81; A61K-39:015  
Publication Language: English  
Fulltext Availability:  
Detailed Description  
Claims  
Fulltext Word Count: 18036

#### English Abstract

This invention relates to an immunogenic composition capable of eliciting an immunogenic response directed to an epitope comprising an isolated Pfs28 and an isolated molecule comprising the epitope. The invention is also directed to methods of eliciting an immunogenic response directed to an epitope comprising administering an isolated Pfs28 and an isolated molecule comprising the epitope. This invention also relates to Pfs25-Pfs28 nucleic acids and fusion proteins. Cells, expression systems, and immunogenic compositions related to the nucleic acids and fusion proteins are provided. Methods of blocking transmission of malarial parasites using compositions of the invention are also provided.

#### French Abstract

L'invention concerne une composition immunogene pouvant provoquer une reponse immunogene dirigee contre un epitope comprenant un Pfs28 isole et contre une molecule isolee comprenant cet epitope. L'invention concerne egalement des procedes destines a provoquer une reponse immunogene dirigee contre un epitope et consistant a administrer Pfs28 isole ainsi qu'une molecule isolee comprenant l'epitope. Cette invention concerne encore des acides nucleiques et des proteines de fusion de Pfs25-Pfs28. On decrit egalement des cellules, systemes d'expression et compositions immunogenes apparentes a ces acides nucleiques et proteines de fusion, ainsi que des procedes de blocage de la transmission de parasites paludeens, dans lesquels on utilise les compositions de l'invention.

7/5/12 (Item 12 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00394264

#### **FIBROBLAST GROWTH FACTOR HOMOLOGOUS FACTOR-3 (FHF-3) AND METHODS OF USE FACTEUR 3 HOMOLOGUE DU FACTEUR DE CROISSANCE DES FIBROBLASTES (FHF-3) ET PROCEDES D'UTILISATION**

Patent Applicant/Assignee:

THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE,

Inventor(s):

NATHANS Jeremy,  
SMALLWOOD Philip M,  
TONG Patrick,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9735007 A1 19970925  
Application: WO 97US4641 19970321 (PCT/WO US9704641)  
Priority Application: US 96621143 19960321

Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES  
FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW  
MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN GH KE LS MW  
SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT  
LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Main International Patent Class: C12N-015/12

International Patent Class: C12N-15:18; C07K-14:50

Publication Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 15882

#### English Abstract

A novel protein, fibroblast growth factor homologous factor-3 (FHF-3), the polynucleotide sequence encoding FHF-3, and the deduced amino acid sequence are disclosed. Also disclosed are diagnostic and therapeutic methods of using the FHF-3 polypeptide and polynucleotide sequences and antibodies which specifically bind to FHF-3.

#### French Abstract

L'invention concerne une proteine nouvelle, le facteur 3 homologue du facteur de croissance des fibroblastes (FHF-3), la sequence polynucleotidique codant FHF-3 et la sequence d'acides amines derivee. L'invention a egalement pour objet des procedes diagnostiques et therapeutiques d'utilisation des sequences polypeptidiques et polynucleotidiques FH-3 et d'anticorps qui se lient specifiquement a FH-3.

7/5/13 (Item 13 from file: 349)

DIALOG(R) File 349: PCT FULLTEXT

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00372119 \*\*Image available\*\*

#### **MERCAPTOAMIDE DERIVATIVES AND THEIR THERAPEUTIC USE**

#### **DERIVES MERCAPTOAMIDE ET LEUR UTILISATION THERAPEUTIQUE**

Patent Applicant/Assignee:

CHIROSCIENCE LIMITED,  
BAXTER Andrew Douglas,  
MONTANA John,  
WATSON Robert John,  
TIFFIN Peter David,

Inventor(s):

BAXTER Andrew Douglas,  
MONTANA John,  
WATSON Robert John,  
TIFFIN Peter David,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9712861 A1 19970410

Application: WO 96GB2439 19961004 (PCT/WO GB9602439)

Priority Application: GB 9520360 19951005; GB 9525648 19951215

Designated States: AL AM AU AZ BA BB BG BR BY CA CN CZ EE GB GE HU IL IS JP KE  
KG KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK  
TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM  
AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA  
GN ML MR NE SN TD TG

Main International Patent Class: C07D

International Patent Class: C07C; C07C; A61K-31:415; A61K-31:22; A61K-31:16

Publication Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 8905

## English Abstract

Mercaptoamide derivatives of formula (I), in which Y represents CHOH, CHNH<sub>2</sub> or C=O and the other variables are defined in the description, have therapeutic activity as metalloproteinase, TNFalpha and L-selectin sheddase inhibitors.

## French Abstract

Cette invention se rapporte a des derives mercaptoamide representes par la formule (I), dans laquelle Y represente CHOH, CHNH<sub>2</sub> ou C=O et ou les autres variables sont definies dans le descriptif. Ces derives ont une activite therapeutique en tant qu'inhibiteurs de metalloproteases, du facteur de necrose tumorale alpha (TNF'alpha') et de la L-selectine sheddase.

7/5/14 (Item 14 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00331103

**BCL-X/BCL-2 ASSOCIATED CELL DEATH REGULATOR**

**REGULATEUR DE LA MORT CELLULAIRE ASSOCIE AUX PROTEINES BCL-2 ET BCL-X**

Patent Applicant/Assignee:

WASHINGTON UNIVERSITY,

KORSMEYER Stanley J,

Inventor(s):

KORSMEYER Stanley J,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9613614 A1 19960509

Application: WO 95US14246 19951031 (PCT/WO US9514246)

Priority Application: US 94333565 19941031

Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU

IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU

SD SE SG SI SK TJ TM TT UA UG US UZ VN KE LS MW SD SZ UG AT BE CH DE DK

ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD

TG

Main International Patent Class: C12Q-001/68

International Patent Class: G01N-33:574; C08L-97:00; C07H-21:02; C07H-21:04

Publication Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 35352

## English Abstract

The invention provides novel compositions, methods, and uses of Bad polypeptides and polynucleotides.

## French Abstract

L'invention se rapporte a de nouveaux procedes, de nouvelles compositions et utilisations des polypeptides et polynucleotides Bad.

7/5/15 (Item 15 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00328699 \*\*Image available\*\*

**PEPTIDYL COMPOUNDS AND THEIR THERAPEUTIC USE AS INHIBITORS OF METALLOPROTEASES**

**COMPOSES DE PEPTIDYLE ET LEUR USAGE THERAPEUTIQUE EN TANT QU'INHIBITEURS DES METALLOPROTEASES**

Patent Applicant/Assignee:

CHIROSCIENCE LIMITED,

Inventor(s):

MONTANA John,  
BAXTER Andrew Douglas,  
OWEN David Alan,  
WATSON Robert John,  
PHILLIPSON Neil,

## Patent and Priority Information (Country, Number, Date):

Patent: WO 9611209 A1 19960418  
Application: WO 95GB2362 19951005 (PCT/WO GB9502362)  
Priority Application: GB 9420057 19941005; GB 954907 19950310; GB 959431 19950510

Designated States: AM AU BB BG BR BY CA CN CZ EE FI GB GE HU IS JP KE KG KP  
KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TT UA  
UG UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE  
BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Main International Patent Class: C07K-005/06

International Patent Class: A61K-38:05

Publication Language: English

Fulltext Availability:

Detailed Description

Claims

Fulltext Word Count: 21934

## English Abstract

Compounds of general formula (I) have utility as inhibitors of matrix metalloproteinases and TNF.

## French Abstract

Les composés de peptidyle de la formule générale (I) sont utiles en tant qu'inhibiteurs des metalloproteases matricielles et du TNF (facteur de necrose tumorale).

?

Set	Items	Description
S1	8	CANCER-ASSOCIATED PROTEIN
S2	4	RD (unique items)
S3	0	ABOUT 28KD
S4	313	28KD
S5	90	S4 AND CANCER
S6	15	S5 AND BREAST
S7	15	RD (unique items)
?		

T S22/5/ALL

22/5/1 (Item 1 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

13608099 BIOSIS NO.: 200200236920

**Generation of monoclonal antibody CIBCgp185 against C-erbB-2 oncoprotein and its clinical evaluation.**

AUTHOR: Meenakshi A(a); Kumar R Suresh; Kumar N Siva  
AUTHOR ADDRESS: (a) Department of Biochemical Oncology, Cancer Institute (WIA), Chennai, 600020\*\*India E-Mail: caninst@md2.vsnl.net.in  
JOURNAL: Human Antibodies 10 (3-4):p101-107 2001  
MEDIUM: print  
ISSN: 1093-2607  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** The C-erbB-2 proto-oncogene encodes the production of a cell surface receptor **protein**, with tyrosine kinase activity. Over expression of this gene either due to gene amplification and/or increased transcription has been observed and has been correlated with poor prognosis in patients with Breast (10-33%) and ovarian (20-33%) cancers. The very low levels of expression of C-erbB-2 by normal tissues makes this receptor a potential target for **diagnosis** and therapy with Monoclonal antibodies raised against its extracellular domain. One such monoclonal antibody designated as CIBCgp185 of IgG2a isotype has been generated in our laboratory using BT474 breast carcinoma cell line as immunogen. This monoclonal antibody immunoprecipitated a 185KD glycoprotein. The specificity of this antibody was confirmed by the formation of a single discrete band and positive reaction with BT474 antigen in Western blot and Dot blot respectively. Flowcytometric analysis performed using various cancer cell lines revealed that this Monoclonal antibody exhibited high binding affinity with BT474 and SKBR3 cells which overexpresses C-erbB-2. By immunoperoxidase test, this antibody stained specifically the tumor cell membrane in frozen tissue sections of breast and ovarian tumors indicating overexpression of the C-erbB-2 product. All these results well correlated with those obtained using a control antibody ICR12, an anti-C-erbB-2 antibody. These studies clearly indicate that Monoclonal antibody CIBCgp185 might prove useful to identify tumors with over expression of C-erbB-2 which are often associated with poor prognosis and early recurrence.

REGISTRY NUMBERS: 80449-02-1: TYROSINE KINASE

**DESCRIPTORS:**

MAJOR CONCEPTS: Immune System (Chemical Coordination and Homeostasis); Membranes (Cell Biology); Molecular Genetics (Biochemistry and Molecular Biophysics)  
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia  
ORGANISMS: BT474 cell line (Hominidae)--human breast cancer cells  
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
DISEASES: **breast cancer** --neoplastic disease, reproductive system disease/female; ovarian cancer--neoplastic disease, reproductive system disease/female  
CHEMICALS & BIOCHEMICALS: C-erbB-2--monoclonal antibody, proto-oncogene; CIBCgp-185--monoclonal antibody; tyrosine kinase  
ALTERNATE INDEXING: Breast Neoplasms (MeSH); Ovarian Neoplasms (MeSH)  
CONCEPT CODES:  
10508 Biophysics-Membrane Phenomena  
03502 Genetics and Cytogenetics-General  
03508 Genetics and Cytogenetics-Human  
10802 Enzymes-General and Comparative Studies; Coenzymes

16506 Reproductive System-Pathology  
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects;  
Systemic Effects  
34502 Immunology and Immunochemistry-General; Methods  
BIOSYSTEMATIC CODES:  
86215 Hominidae

22/5/2 (Item 2 from file: 5)  
DIALOG(R) File 5:Biosis Previews(R)  
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13606087 BIOSIS NO.: 200200234908  
**Synthetic peptides identified from phage-displayed combinatorial libraries as immunodiagnostic assay surrogate quality-control targets.**  
AUTHOR: Sompuram Seshi R(a); Kodela Vani; Ramanathan Halasya; Wescott Charles; Radcliffe Gail; Bogen Steven A  
AUTHOR ADDRESS: (a) CytoLogix Corporation, 99 Erie St, Cambridge, MA, 02139  
\*\*USA E-Mail: ssompuram@cytologix.com  
JOURNAL: Clinical Chemistry 48 (3):p410-420 March, 2002  
MEDIUM: print  
ISSN: 0009-9147  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** Background: Quantitative immunohistochemical (IHC) assays currently lack optimal reference quality-control material for cellular **proteintargets**. To address this problem, we identified peptides that mimic the site on the native analyte to which the primary (monoclonal) antibody binds and used them as surrogate peptide controls. Methods: We identified peptide candidates from a combinatorial peptide phage-display library that mimic the epitope for the 1D5 estrogen receptor (ER) monoclonal antibody (mAb). The peptide inserts of the phage clones were sequenced. Several phage-encoded peptides were then synthesized and analyzed for affinity and specificity. Results: We identified phage clones that specifically bound to the ER 1D5 mAb. The binding was specific, in that the phage clones did not bind to two other isotype-matched mAbs. Their ability to bind the ER 1D5 mAb was related to the presence of a consensus sequence. Binding analysis revealed a  $K_{dof}$  of  $8.3 \times 10^{-8}$  mol/L. The peptide was not recognized by any of 15 other mAbs commonly used for clinical IHC testing. Moreover, the peptide was able to inhibit the binding of ER 1D5 mAb to native ER, indicating that the peptide bound to ER 1D5 mAb at or close to the antigen-binding site. Conclusions: Surrogate peptide controls behave like the native analyte in terms of affinity and specificity. This technology may be especially useful when the native analyte is in short supply.

**DESCRIPTORS:**

MAJOR CONCEPTS: Methods and Techniques; Oncology (Human Medicine, Medical Sciences)  
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Viruses--Microorganisms  
ORGANISMS: human (Hominidae); phage (Viruses)  
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Microorganisms; Primates; Vertebrates; Viruses  
DISEASES: **breast cancer** -- diagnosis , neoplastic disease, reproductive system disease/female  
CHEMICALS & BIOCHEMICALS: 1D5 estrogen receptor monoclonal antibody; estrogen receptor; peptide  
METHODS & EQUIPMENT: quantitative immunohistochemistry--**diagnostic** method  
MISCELLANEOUS TERMS: phage-displayed combinatorial library  
ALTERNATE INDEXING: Breast Neoplasms (MeSH)  
CONCEPT CODES:



10064 Biochemical Studies-Proteins, Peptides and Amino Acids  
12504 Pathology, General and Miscellaneous-Diagnostic  
16506 Reproductive System-Pathology  
24001 Neoplasms and Neoplastic Agents-Diagnostic Methods  
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects;  
Systemic Effects

## BIOSYSTEMATIC CODES:

02500 Viruses-General (1993- )  
86215 Hominidae

22/5/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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13371112 BIOSIS NO.: 200100578261

**Changes in the expression and binding properties of the estrogen receptor in MCF-7 breast cancer cells during growth inhibition by tamoxifen and cisplatin.**

AUTHOR: Otto Angela M(a); Schubert Sybilla; Netzker Roland

AUTHOR ADDRESS: (a)Heinz-Nixdorf-Lehrstuhl fuer Medizinische Elektronik,  
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angela.otto@ei.tum.de\*\*Germany

JOURNAL: Cancer Chemotherapy and Pharmacology 48 (4):p305-311 October,  
2001

MEDIUM: print

ISSN: 0344-5704

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Most mammary carcinomas contain estrogen receptors (ER), which are an important factor in diagnosis and prognosis, and in deciding on the type of therapy. ER-positive tumors are most commonly treated with the antiestrogen tamoxifen or with a combination of chemotherapeutic drugs. An important aspect for further treatment and anticipating possible side effects is the fate of the ER during the course of therapy. To study the effect of drug-induced growth inhibition on ER expression and binding properties, human breast cancer MCF-7 cells were treated with tamoxifen and cisplatin, and also estradiol (E2) for 5 days. Following this incubation, intact cells were incubated with (3H)E2 to determine the dissociation constant (KD) and maximal number of binding sites (Bmax) of the ER. The amount of ER protein per cell was quantified using anti-ER antibodies. For analysis of ER mRNA, total cellular RNA was subjected to Northern blotting. The 5-day treatment with E2 reduced Bmax and the amount of ER protein by about 70%, while the cellular level of ER mRNA was reduced by 40%. Treatment with E2 did not affect the subsequent growth inhibitory response to tamoxifen or cisplatin. In contrast, tamoxifen reduced the capacity for E2 binding; it caused about a 30-fold increase in the KD value. At the same time, Bmax and ER protein content were increased (about 3.5- and 2-fold, respectively), but the cellular level of ER mRNA was again reduced by 40%. The growth of tamoxifen-treated cells remained sensitive to subsequent treatment with estradiol, tamoxifen or cisplatin. Treatment of MCF-7 cells with cisplatin likewise reduced E2 binding due to a 20-fold increase in KD value. In this case, both Bmax and the amount of ER protein were decreased when calculated per milligram of protein, but were increased on a cellular basis due to an increase in cell size. The ER mRNA content was not altered in cisplatin-treated cells. Growth of these cells also remained sensitive to tamoxifen and cisplatin. In conclusion, drug-induced changes in ER expression and binding capacity do not necessarily indicate a loss of sensitivity of breast cancer cells to a subsequent chemotherapeutic treatment.

REGISTRY NUMBERS: 15663-27-1: CISPLATIN; 50-28-2: ESTRADIOL; 10540-29-1: TAMOXIFEN

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Reproductive System (Reproduction); Tumor Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: MCF-7 cell line (Hominidae)--growth inhibition, human breast cancer cell line

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: **breast cancer** --neoplastic disease, reproductive system disease/female; **mammary carcinoma**--neoplastic disease, reproductive system disease/female

CHEMICALS & BIOCHEMICALS: **cisplatin**--antineoplastic-drug; **estradiol**; **estrogen**; **estrogen receptor**--binding properties, expression; **tamoxifen**--antineoplastic-drug

ALTERNATE INDEXING: Breast Neoplasms (MeSH); Mammary Neoplasms (MeSH); Carcinoma (MeSH)

CONCEPT CODES:

- 02508 Cytology and Cytochemistry-Human
- 10060 Biochemical Studies-General
- 10064 Biochemical Studies-Proteins, Peptides and Amino Acids
- 10067 Biochemical Studies-Sterols and Steroids
- 12512 Pathology, General and Miscellaneous-Therapy (1971- )
- 16504 Reproductive System-Physiology and Biochemistry
- 16506 Reproductive System-Pathology
- 22002 Pharmacology-General
- 22005 Pharmacology-Clinical Pharmacology (1972- )
- 24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
- 24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy

BIOSYSTEMATIC CODES:

- 86215 Hominidae

22/5/4 (Item 4 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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12277554 BIOSIS NO.: 200000031056

**DOTA-lanreotide: A novel somatostatin analog for tumordiagnosis and therapy.**

AUTHOR: Smith-Jones Peter M; Bischof Claudia; Leimer Maria; Gludovacz Doris ; Angelberger Peter; Pangerl Thomas; Peck-Radosavljevic Markus; Hamilton Gerhard; Kaserer Klaus; Kofler Anne; Schlagbauer-Wadl Hermine; Traub Tatjana; Virgolini Irene(a)

AUTHOR ADDRESS: (a)Department of Nuclear Medicine, University of Vienna, Waehringer Guertel 18-20, Ebene 3L, A-1090, Vienna\*\*Austria

JOURNAL: Endocrinology 140 (11):p5136-5148 Nov., 1999

ISSN: 0013-7227

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Long acting somatostatin-14 (SST) analogs are used clinically to inhibit tumor growth and proliferation of various tumor types via binding to specific receptors (R). We have developed a <sup>111</sup>In-/90Y-labeled SST analog, DOTA-(D)betaNal1-lanreotide (DOTALAN), for tumordiagnosis and therapy. <sup>111</sup>In-/90Y-DOTALAN bound with high affinity (dissociation constant, **K<sub>d</sub>**, 1-12 nM) to a number of primary human tumors (n = 31) such as intestinal adenocarcinoma (n = 17; 150-4000 fmol/mg**protein**) or breast cancer (n = 4; 250-9000 fmol/mg**protein**). <sup>111</sup>In-/90Y-DOTALAN exhibited a similar high binding affinity (**K<sub>d</sub>**, 1-15 nM) for the human

breast cancer cell lines T47D and ZR75-1, the prostate cancer cell lines PC3 and DU145, the colonic adenocarcinoma cell line HT29, the pancreatic adenocarcinoma cell line PANC1, and the melanoma cell line 518A2. When expressed in COS7 cells, <sup>111</sup>In-DOTALAN bound with high affinity to hsst2 (K<sub>d</sub> , 4.3 nM), hsst3 ( K<sub>d</sub> , 5.1 nM), hsst4 ( K<sub>d</sub> , 3.8 nM), and hsst5 ( K<sub>d</sub> , 10 nM) and with lower affinity to hsst1 ( K<sub>d</sub> , apprxx200 nM). The rank order of displacement of (125I)Tyr11-SST binding to hsst1 was: SST (IC<sub>50</sub>, 0.5 nM) mchgt DOTALAN (IC<sub>50</sub>, 154 nM) > lanreotide (LAN) apprxx Tyr3-octreotide (TOCT) apprxx DOTA-Tyr3-octreotide (DOTATOCT) apprxx DOTA-vapreotide (DOTAVAP; IC<sub>50</sub>, >1000 nM); that to hsst2 was: DOTATOCT apprxx TOCT apprxx DOTALAN apprxx SST apprxx LAN apprxx DOTAVAP (IC<sub>50</sub>, 1.4 nM); that to hsst3 was: SST (IC<sub>50</sub>, 1.2 nM) > DOTALAN = LAN (IC<sub>50</sub>, 15 nM) apprxx TOCT (IC<sub>50</sub>, 20 nM) apprxx DOTAVAP (IC<sub>50</sub>, 28 nM) > DOTATOCT (IC<sub>50</sub>, 73 nM); that to hsst4 was: SST (IC<sub>50</sub>, 1.8 nM) apprxx DOTALAN (IC<sub>50</sub>, 2.5 nM) > LAN (IC<sub>50</sub>, 22 nM) mchgt DOTATOCT apprxx DOTAVAP apprxx TOCT (IC<sub>50</sub>, >500 nM); and that to hsst5 was: DOTALAN (IC<sub>50</sub>, 0.45 nM) > SST (IC<sub>50</sub>, 0.9 nM) > TOCT (IC<sub>50</sub>, 1.5 nM) > DOTAVAP (IC<sub>50</sub>, 5.4 nM) mchgt LAN (IC<sub>50</sub>, 21 nM) > DOTATOCT (IC<sub>50</sub>, 260 nM). In Sprague Dawley rats (n = 10), <sup>90</sup>Y-DOTALAN was rapidly cleared from the circulation and concentrated in hsst-positive tissues such as pancreas or pituitary. Taken together, our results indicate that <sup>111</sup>In-/<sup>90</sup>Y-DOTALAN binds to a broad range of primary human tumors and tumor cell lines, probably via binding to hsst2-5. We conclude that this radiolabeled peptide can be used for hsst-mediated **diagnosis** (<sup>111</sup>In-DOTALAN) as well as systemic radiotherapy (<sup>90</sup>Y-DOTALAN) of human tumors.

REGISTRY NUMBERS: 51110-01-1: SOMATOSTATIN-14

DESCRIPTORS:

MAJOR CONCEPTS: Cell Biology; Pharmacology; Tumor Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: 518A2 cell line (Hominidae)--human melanoma cells; COS7 cell line (Hominidae)--African green monkey kidney cells; DU145 cell line (Hominidae)--human prostate cancer cells; HT29 cell line (Hominidae)--human colonic adenocarcinoma cells; PANC1 cell line (Hominidae)--human pancreatic adenocarcinoma cells; PC3 cell line (Hominidae)--human prostate cancer cells; T47D cell line (Hominidae)--human breast cancer cells; ZR75-1 cell line (Hominidae)--human breast cancer cells; human (Hominidae)--patient

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: **breast cancer** --neoplastic disease, reproductive system disease/female; intestinal adenocarcinoma--digestive system disease, neoplastic disease; tumor--**diagnosis** , neoplastic disease, therapy

CHEMICALS & BIOCHEMICALS: DOTA-lanreotide {DOTALAN}--somatostatin analog; somatostatin-14

ALTERNATE INDEXING: Breast Neoplasms (MeSH)

CONCEPT CODES:

22002 Pharmacology-General  
02506 Cytology and Cytochemistry-Animal  
02508 Cytology and Cytochemistry-Human  
06502 Radiation-General  
10060 Biochemical Studies-General  
24002 Neoplasms and Neoplastic Agents-General  
12504 Pathology, General and Miscellaneous-Diagnostic  
12512 Pathology, General and Miscellaneous-Therapy (1971- )  
13002 Metabolism-General Metabolism; Metabolic Pathways

BIOSYSTEMATIC CODES:

86215 Hominidae

22/5/5 (Item 5 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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10837308 BIOSIS NO.: 199799458453

**Overexpression of the oncogene c-erbB-2 (HER2/neu) in ovarian cancer: A new prognostic factor.**

AUTHOR: Meden Harald(a); Kuhn Walter

AUTHOR ADDRESS: (a)Dep. Obstetrics Gynecology, Univ. Goettingen,

Robert-Koch-Str. 40, D-37075 Goettingen\*\*Germany

JOURNAL: European Journal of Obstetrics & Gynecology and Reproductive  
Biology 71 (2):p173-179 1997

ISSN: 0301-2115

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Ovarian cancer is the leading cause of death in gynecological cancers. To date, there are no prognostic factors in ovarian cancer that adequately account for tumor biology and the course of the disease. In recent years, some reports have described the prognostic significance of the amplification and overexpression of the oncogene c-erbB-2 (HER2/neu) in various human cancers, including ovarian cancer. The c-erbB-2 proto-oncogene is located on the long arm of chromosome 17. It encodes a 185kDtransmembrane glycoprotein receptor (p185-HER2) that has sequence similarities with the epidermal growth factor receptor (EGF-R). In ovarian cancer, the percentage of c-erbB-2 positive cases varies from 9 to 32%. Correlation with tumor stage and the degree of histological differentiation was not observed. The overexpression of c-erbB-2 is a new and statistically independent prognostic factor. The overexpression of oncogene c-erbB-2 in ovarian cancer can be detected by immunohistochemistry staining for theproteinp185 and characterizes a group with unfavorable tumor biology and a significantly worse prognosis. Elevated serum levels of the c-erbB-2 oncoprotein have been identified in patients with various cancers known to overexpress the c-erbB-2 oncogene. The detection of a p185 oncoprotein fragment in the sera of ovarian cancer patients was recently published by our group. Antiproliferative effects of monoclonal antibodies directed against p185 have been demonstrated in breast cancer patients. This may lead to a new approach in ovarian carcinoma therapy, too, over and above thediagnostic aspects.

**DESCRIPTORS:**

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Metabolism; Oncology (Human Medicine, Medical Sciences); Pathology; Reproductive System (Reproduction)

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates

MISCELLANEOUS TERMS: Journal Article;**BREAST CANCER** ; C-ERBB-2

ONCOGENE; CHROMOSOME 17; EPIDERMAL GROWTH FACTOR RECEPTOR; NEOPLASTIC DISEASE; ONCOLOGY; OVARIAN CANCER; OVEREXPRESSION; PATIENT; PROGNOSTIC FACTOR; P185-HER2; REPRODUCTIVE SYSTEM DISEASE/FEMALE; TRANSMEMBRANE GLYCOPROTEIN RECEPTOR

**CONCEPT CODES:**

10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

10506 Biophysics-Molecular Properties and Macromolecules

10508 Biophysics-Membrane Phenomena

12510 Pathology, General and Miscellaneous-Necrosis (1971- )

13014 Metabolism-Nucleic Acids, Purines and Pyrimidines

16506 Reproductive System-Pathology

24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects

24006 Neoplasms and Neoplastic Agents-Biochemistry

**BIOSYSTEMATIC CODES:**

86215 Hominidae

22/5/6 (Item 1 from file: 72)  
 DIALOG(R) File 72:EMBASE  
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11717580 EMBASE No: 2002290513

**The HER2 extracellular domain as a prognostic and predictive factor in breast cancer**

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Clinical Breast Cancer ( CLIN. BREAST CANCER ) (United States) 2002,  
 3/2 (125-135)

CODEN: CBCLB ISSN: 1526-8209

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 120

The HER2/neu proto-oncogene encodes a 185-kD transmembrane receptor with tyrosine kinase activity. Amplification of HER2 with overexpression of

the p185<sup>SUPHER2</sup> receptor occurs in 20%-30% of breast cancers and has been established as an independent prognostic factor in numerous studies. Increasing evidence suggests that HER2 may be a predictive marker for response to chemotherapy and hormonal therapy. HER2 overexpression has provided a new target in breast cancer therapy, as evidenced by the development of trastuzumab (Herceptin(R)), a monoclonal antibody targeted against HER2. Detection of HER2 in the clinical setting is performed by immunohistochemistry or fluorescence in situ hybridization in tissue, and by detection of the shed extracellular domain in serum or plasma. Differences in methodology, reagents, and scoring systems have led to varying results in different patient cohorts, contributing to the debate on the role of HER2 as a prognostic and predictive factor. This review focuses on the prognostic and predictive value of serum HER2 detection in the management of HER2-positive breast cancer.

BRAND NAME/MANUFACTURER NAME: herceptin

DEVICE BRAND NAME/MANUFACTURER NAME: HercepTest/Dako/United States; INFORM/Ventana; PathVysion/Vysis/United States

DEVICE MANUFACTURER NAMES: Dako/United States; Ventana; Vysis/United States  
 DRUG DESCRIPTORS:

\*growth factor receptor--endogenous compound--ec; \*oncoprotein--endogenous compound--ec

protein tyrosine kinase--endogenous compound--ec; protein p185  
 --endogenous compound--ec; biological marker--endogenous compound--ec;  
 trastuzumab--adverse drug reaction--ae; trastuzumab--drug combination--cb;  
 trastuzumab--drug development--dv; trastuzumab--drug therapy--dt;  
 trastuzumab--pharmacokinetics--pk; trastuzumab--pharmacology--pd; cisplatin  
 --drug combination--cb; cisplatin--drug interaction--it; cisplatin--drug  
 therapy--dt; cisplatin--pharmacology--pd; thiotepa--drug interaction--it;  
 thiotepa--drug therapy--dt; thiotepa--pharmacology--pd; cyclophosphamide  
 --adverse drug reaction--ae; cyclophosphamide--drug combination--cb;  
 cyclophosphamide--drug comparison--cm; cyclophosphamide--drug interaction  
 --it; cyclophosphamide--drug therapy--dt; cyclophosphamide--pharmacology  
 --pd; methotrexate--drug combination--cb; methotrexate--drug comparison--cm  
 ; methotrexate--drug therapy--dt; methotrexate--pharmacology--pd;  
 fluorouracil--drug combination--cb; fluorouracil--drug comparison--cm;  
 fluorouracil--drug therapy--dt; fluorouracil--pharmacology--pd; doxorubicin  
 --adverse drug reaction--ae; doxorubicin--drug combination--cb; doxorubicin  
 --drug therapy--dt; doxorubicin--pharmacology--pd; mitoxantrone--drug  
 combination--cb; mitoxantrone--drug comparison--cm; mitoxantrone--drug  
 therapy--dt; mitoxantrone--pharmacology--pd; DNA topoisomerase (ATP  
 hydrolysing)--endogenous compound--ec; paclitaxel--drug combination--cb;  
 paclitaxel--drug therapy--dt; paclitaxel--pharmacology--pd; cyclin

dependent kinase 2--endogenous compound--ec; docetaxel--drug therapy--dt;  
 docetaxel--pharmacology--pd; tamoxifen--drug comparison--cm; tamoxifen  
 --drug therapy--dt; tamoxifen--pharmacology--pd; vincristine--drug  
 combination--cb; vincristine--drug therapy--dt; vincristine--pharmacology  
 --pd; prednisone--drug combination--cb; prednisone--drug therapy--dt;  
 prednisone--pharmacology--pd; gemcitabine--drug therapy--dt; gemcitabine  
 --pharmacology--pd; megestrol acetate--drug therapy--dt; megestrol acetate  
 --pharmacology--pd; fadrozole--drug therapy--dt; fadrozole--pharmacology  
 --pd; droloxifene--drug therapy--dt; droloxifene--pharmacology--pd;  
 letrozole--drug comparison--cm; letrozole--drug therapy--dt; letrozole  
 --pharmacology--pd; navelbine--drug combination--cb; navelbine--drug  
 therapy--dt; navelbine--pharmacology--pd; unclassified drug

# MEDICAL DESCRIPTORS:

\*breast cancer --drug therapy--dt; \* breast cancer --etiology--et; \*  
 breast cancer --therapy--th; \*oncogene neu  
 proteindomain; prognosis; prediction; enzyme activity; gene  
 amplification; gene overexpression; cancer chemotherapy; hormonal therapy;  
 drug targeting;proteinanalysis; immunohistochemistry; fluorescence in  
 situ hybridization;proteinlocalization; protein blood level;  
 diagnostickit; autologous bone marrow transplantation; cardiotoxicity  
 --side effect--si; sensitivity and specificity; human; nonhuman; mouse;  
 major clinical study; controlled study; animal tissue; review

DRUG TERMS (UNCONTROLLED):proteinher 2--endogenous compound--ec

CAS REGISTRY NO.: 80449-02-1 (proteintyrosine kinase); 180288-69-1 (  
 trastuzumab); 15663-27-1, 26035-31-4, 96081-74-2 (cisplatin); 52-24-4 (  
 thiotepa); 50-18-0 (cyclophosphamide); 15475-56-6, 59-05-2, 7413-34-5 (  
 methotrexate); 51-21-8 (fluorouracil); 23214-92-8, 25316-40-9 (  
 doxorubicin); 65271-80-9, 70476-82-3 (mitoxantrone); 33069-62-4 (  
 paclitaxel); 141349-86-2 (cyclin dependent kinase 2); 114977-28-5 (  
 docetaxel); 10540-29-1 (tamoxifen); 57-22-7 (vincristine); 53-03-2 (  
 prednisone); 103882-84-4 (gemcitabine); 595-33-5 (megestrol acetate);  
 102676-31-3 (fadrozole); 82413-20-5 (droloxifene); 112809-51-5 (  
 letrozole); 71486-22-1 (navelbine)

# SECTION HEADINGS:

016 Cancer  
 027 Biophysics, Bioengineering and Medical Instrumentation  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reaction Titles

22/5/7 (Item 2 from file: 72)

DIALOG(R) File 72:EMBASE

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11646515 EMBASE No: 2002218313

# Nuclear matrix proteins as biomarkers for breast cancer

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Expert Review of Molecular Diagnostics ( EXPERT REV. MOL. DIAGN. ) (  
 United Kingdom) 2002, 2/1 (23-31)

CODEN: ERMDC ISSN: 1473-7140

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 80

Breast cancer remains a leading cause of cancer death in women despite  
 widespread screening, in part because screening mammography has high rates  
 of false-negative results and because many women decline to have routine  
 mammograms. The development of sensitive and specific assays for breast  
 tumor markers would improve detection and facilitate screening,diagnosis  
 , therapeutic monitoring and surveillance for recurrence. Nuclear matrix  
 proteins (NMPs) are promising candidates for tumor markers because they are

involved in malignant transformation. Therefore, they may be useful for screening and early **diagnosis** of small tumors. Proteomic analysis was used to demonstrate that a 28.3kD serum protein, designated NMP66, can distinguish malignant disease from benign conditions and normal controls. NMP66 is now being evaluated as a potential biomarker for early breast cancer detection in large-scale clinical trials.

DEVICE BRAND NAME/MANUFACTURER NAME: NMP22 Test Kit/Matritech/United States  
 DEVICE MANUFACTURER NAMES: Matritech/United States

DRUG DESCRIPTORS:

\*biological marker; \*matrix **protein**; \*nuclear protein  
 plasmaprotein; trastuzumab; unclassified drug

MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di  
 cancer **diagnosis**; cancer screening; mammography; diagnostic accuracy;  
**diagnostic** value; cancer recurrence; malignant transformation; early  
**diagnosis**; proteomics; cancer incidence; cancer mortality; human; female;  
 clinical trial; review

DRUG TERMS (UNCONTROLLED): nuclear matrix **protein** 66

CAS REGISTRY NO.: 180288-69-1 (trastuzumab)

SECTION HEADINGS:

016 Cancer  
 029 Clinical and Experimental Biochemistry

22/5/8 (Item 3 from file: 72)  
 DIALOG(R) File 72:EMBASE  
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11513623 EMBASE No: 2002084368

**Expression of oestrogen receptor beta (ERbetaI) protein in human breast cancer biopsies**

Saunders P.T.K.; Millar M.R.; Williams K.; Macpherson S.; Bayne C.;  
 O'Sullivan C.; Anderson T.J.; Groome N.P.; Miller W.R.  
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 British Journal of Cancer ( BR. J. CANCER ) (United Kingdom) 21 JAN  
 2002, 86/2 (250-256)  
 CODEN: BJCAA ISSN: 0007-0920  
 DOCUMENT TYPE: Journal ; Article  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 41

Oestrogen action is mediated via specific receptors that act as ligand-activated transcription factors. A monoclonal antibody specific to the C-terminus of human oestrogen receptor beta has been characterized and the prevalence of expression of oestrogen receptor beta **protein** investigated in a well defined set of breast cancers. Reverse transcription-polymerase chain reaction analysis of RNA from tissue biopsies detected oestrogen receptor beta in all samples examined. The anti-oestrogen receptor beta antibody cross reacted specifically with both long ((similar) 59Kd) and short ((similar) 53 Kd) forms of recombinant oestrogen receptor beta. Western blot analysis of breast tumours contained both forms of oestrogen receptor beta **protein** although in some samples lower molecular weight species (32-45Kd) were identified. Fifty-one breast cancer biopsies were examined using immunohistochemistry; 41 (80%) were immunopositive for oestrogen receptor alpha, 48 (94%) were immunopositive for oestrogen receptor beta and 38 (74.5%) co-expressed both receptors. Expression of oestrogen receptor beta was exclusively nuclear and occurred in multiple cell types. There was no quantitative relationship between staining for the two ERs although in tumours in which both receptors were present immunoreexpression of oestrogen receptor alpha was invariably more intense. The significance of oestrogen receptor beta **protein** expression in breast cancers to therapy remains to be determined

but the availability of a well characterized antibody capable of detecting oestrogen receptor beta in archive material will facilitate the process.

(c) 2002 The Cancer Research Campaign.

#### DRUG DESCRIPTORS:

\*estrogen receptor beta--endogenous compound--ec; \*estrogen--endogenous compound--ec; \*transcription factor--endogenous compound--ec; \*monoclonal antibody--endogenous compound--ec; \*estrogen receptor alpha--endogenous compound--ec

#### MEDICAL DESCRIPTORS:

\***protein**expression; \* breast cancer -- diagnosis --di breast biopsy; estrogen activity; carboxy terminal sequence; reverse transcription polymerase chain reaction; Western blotting; immunohistochemistry; human; major clinical study; human tissue; human cell ; article; priority journal

#### SECTION HEADINGS:

005 General Pathology and Pathological Anatomy  
016 Cancer

22/5/9 (Item 4 from file: 72)

DIALOG(R) File 72:EMBASE

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07711201 EMBASE No: 1999194663

**Construction and characterization of a chimeric fusionprotein consisting of an anti-idiotypic antibody mimicking a breast cancer-associated antigen and the cytokine GM-CSF**

Tripathi P.K.; Qin H.; Bhattacharya-Chatterjee M.; Ceriani R.L.; Foon K.A.; Chatterjee S.K.

Dr. S.K. Chatterjee, 204 Combs Research Building, Markey Cancer Center, University of Kentucky, Lexington, KY 40536-0096 United States  
Hybridoma ( HYBRIDOMA ) (United States) 1999, 18/2 (193-202)

CODEN: HYBRD ISSN: 0272-457X

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 41

Anti-idiotypic antibody, 11D10 mimics biologically and antigenically a distinct and specific epitope of the high molecular weight human milk fat globule (HMFG), a cancer-associated antigen present in over 90% of breast tumor samples. To augment the immunogenicity of 11D10 without the aid of a carrierproteinor adjuvant, we made a chimeric 11D10-GM-CSF fusion proteinfor use as a vaccine. An expression plasmid for 11D10 was made by ligation of the DNA sequences of the 11D10 light-chain variable region upstream of the human kappa constant region. The heavy-chain plasmid carrying GM-CSF was made by ligation of the heavy-chain variable region sequences upstream of the human gamma1 constant region CH1 fused to the DNA fragment encoding the mature GM-CSF peptide 3' to the CH3 exon. NS1 plasmacytoma cells were transfected with the light and heavy-chain vectors by electroporation. Fusionproteinsecreted in the culture medium was purified and was characterized by gel electrophoresis as well as by determination of the biological activity of the fused GM-CSF. In nonreducing SDS-polyacrylamide gels, a single band ~200Kdreacted with anti-human kappa, anti-human lambda1 and anti-GM-CSF antibodies. In reducing polyacrylamide gels, a ~74kd proteinreacted with antihuman lambda1 and anti- GM-CSF antibodies. The fusionproteininduced proliferation of GM-CSF dependent NFS-60 cells. These results suggest that theproteinis a chimeric anti-idiotypic antibody consisting of 11D10 variable domains, human kappa and lambda1 constant domains and that the GM-CSF moiety fused to the constant region lambda1 is biologically active.

#### DRUG DESCRIPTORS:

\*tumor antigen--endogenous compound--ec; \*granulocyte macrophage colony stimulating factor--pharmacology--pd; \*cytokine--pharmacology--pd; \*cancer



vaccine--pharmacology--pd; \*antiidiotypic antibody--endogenous compound--ec  
 ; \*hybridprotein --pharmacology--pd  
 DNA fragment--endogenous compound--ec; polyacrylamide gel; epitope  
 MEDICAL DESCRIPTORS:  
 \*chimera; \*proteinanalysis; \* breast cancer -- diagnosis --di; \* breast  
 cancer --therapy--th; \*immunogenicity; \*immunotherapy  
 molecular weight; DNA sequence; plasmid; sequence analysis; plasma cell;  
 genetic transfection; electroporation;proteinpurification;  
 electrophoresis; human; article; priority journal  
 SECTION HEADINGS:  
 016 Cancer  
 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index

22/5/10 (Item 5 from file: 72)  
 DIALOG(R)File 72:EMBASE  
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07589038 EMBASE No: 1999070648  
**Immunologic proliferation marker Ki-S2 as prognostic indicator for lymph  
 node-negative breast cancer**  
 Rudolph P.; Alm P.; Heidebrecht H.-J.; Bolte H.; Ratjen V.; Baldetorp B.;  
 Ferno M.; Olsson H.; Parwaresch R.  
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 AUTHOR EMAIL: prudolph@path.uni-kiel.de  
 Journal of the National Cancer Institute ( J. NATL. CANCER INST. ) (   
 United Kingdom) 03 FEB 1999, 91/3 (271-278)  
 CODEN: JNCIA ISSN: 0027-8874  
 DOCUMENT TYPE: Journal; Article  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 52

Background: Proper treatment of lymph node-negative breast cancer depends  
 on an accurate prognosis. To improve prognostic models for this disease, we  
 evaluated whether an immunohistochemical marker for proliferating cells,  
 Ki-S2 (a monoclonal antibody that binds to a 100-kDnuclear protein  
 expressed in S, Ginf 2, and M phases of the cell cycle), is an accurate  
 indicator of prognosis. Methods: We studied 371 Swedish women with lymph  
 node-negative breast cancer; the median follow-up time was 95 months. The  
 fraction of tumor cells in S phase was assessed by flow cytometry, and  
 tumor cell proliferation was measured immunohistochemically with the  
 monoclonal antibodies Ki-S2 and Ki-S5 (directed against the nuclear antigen  
 Ki-67). A combined prognostic index was calculated on the basis of the  
 S-phase fraction, progesterone receptor content, and tumor size. Results:  
 In multivariate analyses that did or did not (263 and 332 observations,  
 respectively) include the S-phase fraction and the combined prognostic  
 index, the Ki-S2 labeling index (percentage of antibody-stained tumor cell  
 nuclei) emerged as the most statistically significant predictor of overall  
 survival, disease-specific survival, and disease-free survival (all  
 two-sided P<.0001). In the risk group defined by a Ki-S2 labeling index of  
 10% or less, life expectancy was not statistically significantly different  
 from that of age- matched women without breast cancer, whereas the group  
 with a high Ki-S2 labeling index had an increased risk of mortality of up  
 to 20-fold. Conclusions: Cellular proliferation is a major determinant of  
 the biologic behavior of breast cancer. Prognosis is apparently best  
 indicated by the percentage of cells in S through M phases of the cell  
 cycle. Measurement of the Ki-S2 labeling index of a tumor sample may  
 improve a clinician's ability to make an accurate prognosis and to identify  
 patients with a low risk of recurrence who may not need adjuvant therapy.

DRUG DESCRIPTORS:  
 \*monoclonal antibody; \*cell nucleus antigen--endogenous compound--ec  
 progesterone receptor--endogenous compound--ec  
 MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \*lymph node metastasis--complication--co  
 ; \*lymph node metastasis--**diagnosis** --di  
 accuracy; cell cycle phase; cell cycle s phase; tumor volume; cell  
 proliferation; cancer survival; prediction; life expectancy; survival rate;  
 labeling index; prognosis; disease marker; human; female; major clinical  
 study; aged; adult; article; priority journal  
 DRUG TERMS (UNCONTROLLED): monoclonal antibody ki s2; monoclonal antibody  
 ki s5

## SECTION HEADINGS:

005 General Pathology and Pathological Anatomy  
 016 Cancer

22/5/11 (Item 6 from file: 72)  
 DIALOG(R) File 72:EMBASE  
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07572989 EMBASE No: 1999059693

**Antiamphiphysin antibodies are associated with various paraneoplastic neurological syndromes and tumors**

Antoine J.C.; Absi L.; Honnorat J.; Boulesteix J.-M.; De Brouker T.; Vial  
 C.; Butler M.; De Camilli P.; Michel D.

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 Pasteur, 42 055 Saint-Etienne Cedex France

Archives of Neurology ( ARCH. NEUROL. ) (United States) 1999, 56/2  
 (172-177)

CODEN: ARNEA ISSN: 0003-9942

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 20

Background: Antiamphiphysin antibodies react with a 128-kd **protein** found in synaptic vesicles. They were first described in patients with paraneoplastic stiff-man syndrome and breast cancer, but studies suggest that they can also occur in patients with other tumors and neurological disorders. Objective: To determine if antiamphiphysin antibodies are associated with various paraneoplastic neurological syndromes and tumors. Patients and Methods: Of 2800 serum samples tested by routine immunohistochemical procedures on sections of paraformaldehyde-fixed rat brain for the detection of autoantibodies associated with paraneoplastic neurological syndromes, 5 were selected because of labeling suggestive of antiamphiphysin antibodies and subsequently confirmed by the results of Western blot analysis using recombinant amphiphysin**protein**. Controls consisted of 40 patients with various nonparaneoplastic neurological diseases; 101 patients with cancer but without paraneoplastic neurological syndrome; 9 patients with small cell lung cancer, anti-Hu antibodies, and paraneoplastic neurological syndrome; 3 patients with Minf 2-type antimitochondrial antibodies but no neurological disorder; and 30 normal subjects. Results: Of the 5 patients with antiamphiphysin antibodies, patient 1 had sensory neuronopathy, encephalomyelitis, and breast cancer; patient 2 had limbic encephalitis, and small cell lung cancer was detected in the mediastinum after 24 months of follow-up; patient 3 had encephalomyelitis and ovarian carcinoma; and patients 4 and 5 had Lambert-Eaton myasthenic syndrome and small cell lung cancer (patient 4 subsequently developed cerebellar degeneration). None of the 5 had stiffness. Two patients (Nos. 2 and 4) had antimitochondrial antibodies. The two patients (Nos. 4 and 5) with Lambert-Eaton myasthenic syndrome had antibodies directed against the voltage-gated calcium channel, and patient 2 subsequently developed anti-Hu antibodies. In the controls, antiamphiphysin antibodies were detected by Western blot analysis in 3 of 8 patients with anti-Hu antibodies, but in none of the other groups. Conclusions: These data indicate that antiamphiphysin antibodies are not specific for one type of tumor or one neurological syndrome and can be associated with other neural and nonneural antibodies. The simultaneous association of several antibodies in some patients suggests multimodal.

autoantibody production.

DRUG DESCRIPTORS:

\*autoantibody--endogenous compound--ec

MEDICAL DESCRIPTORS:

\*paraneoplastic syndrome--**diagnosis** --di; \* breast cancer -- diagnosis --di; \*Eaton Lambert syndrome--**diagnosis** --di; \*lung small cell cancer--**diagnosis** --di

antibody detection; disease association; synapse vesicle;**diagnostic** value;**diagnostic**accuracy; encephalomyelitis-- diagnosis --di; human; male; female; clinical article; aged; adult; article; priority journal

SECTION HEADINGS:

008 Neurology and Neurosurgery

22/5/12 (Item 7 from file: 72)

DIALOG(R)File 72:EMBASE

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07135688 EMBASE No: 1998002010

**Mitosin (a new proliferation marker) correlates with clinical outcome in node-negative breast cancer**

Clark G.M.; Allred D.C.; Hilsenbeck S.G.; Chamness G.C.; Osborne C.K.; Jones D.; Lee W.-H.

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Cancer Research ( CANCER RES. ) (United States) 1997, 57/24 (5505-5508)

CODEN: CNREA ISSN: 0008-5472

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 19

Tumor proliferation rate is an important prognostic factor in breast cancer, and S-phase fraction (SPF), as measured by flow cytometry, is the most clinically validated of several methods for measuring it. However, flow cytometry is not well suited to evaluating the formalin-fixed, paraffin- embedded tumors that are routinely available or to the increasing number of small breast cancers. These and other limitations have motivated research into alternative methods for measuring proliferation, including immunohistochemistry (IHC) against cell cycle-related antigens, which are better suited for the evaluation of small archival tissue samples. Mitosin is a recently described 350kD nuclear phosphoprotein that is expressed in the late Ginf 1, S, Ginf 2, and M phases of the cell cycle but not in Ginf 0. Using a new monoclonal antibody (14C10), this pilot study evaluated mitosin expression by IHC in a series of 386 node-negative, formalin-fixed, archival breast cancers and correlated the results with several prognostic factors and clinical outcome (median follow-up, 78 months; range 3-214 months). The median and range of mitosin positive cells were 7% and 1-47%, respectively. There was a strong positive correlation between mitosin and SPF ( $r = 0.57$ ;  $P = 0.0001$ ), and there were significant negative correlations with estrogen receptor, progesterone receptor, and patient age. Mitosin was not related to overall survival in this pilot study. However, in a univariate cutpoint analysis of disease-free survival (DFS), patients with high levels of mitosin (>9% positive cells) had significantly worse DFS than did patients with lower levels (68% versus 84% at 5 years, respectively). In a multivariate analysis of DFS, large tumor size (>2 cm) and high mitosin were the only independently significant predictors of recurrence (relative risks = 2.47 and 1.72, respectively) in a model containing the additional factors estrogen receptor, progesterone receptor, patient age, and SPF. These preliminary results suggest that mitosin as assessed by IHC may be superior to SPF as a prognostic factor in node-negative breast cancer, but additional studies are necessary to validate these promising findings.

## DRUG DESCRIPTORS:

\*phosphoprotein  
monoclonal antibody; unclassified drug

## MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \* breast cancer --etiology--et  
cell proliferation; prognosis; flow cytometry; immunohistochemistry;  
proteinphosphorylation; protein expression; follow up; prediction; cell  
cycle s phase;diagnosticvalue; human; nonhuman; female; mouse; human  
tissue; human cell; animal tissue; animal cell; aged; adult; article;  
priority journal  
DRUG TERMS (UNCONTROLLED): mitosin; cell nucleus phosphoprotein; monoclonal  
antibody 14c10  
SECTION HEADINGS:  
016 Cancer

22/5/13 (Item 8 from file: 72)

DIALOG(R) File 72:EMBASE

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06586235 EMBASE No: 1996250859

**Detection of bone sialoprotein in human breast cancer tissue and cell  
lines at bothprotein and messenger ribonucleic acid levels**

Bellahcene A.; Antoine N.; Clausse N.; Tagliabue E.; Fisher L.W.; Kerr  
J.M.; Jares P.; Castronovo V.

Metastasis Research Laboratory, Univ. Liege Tour de Pathologie-1, Sart  
Tilman via Liege 4000,Liege Belgium  
Laboratory Investigation ( LAB. INVEST. ) (United States) 1996, 75/2  
(203-210)

CODEN: LAINA ISSN: 0023-6837

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The recent demonstration that bone sialoprotein (BSP) can be detected in human breast cancer tissue by immunoperoxidase suggests that this phosphoprotein is ectopically expressed by malignant mammary epithelial cells. Its detection in human breast cancer cells raises questions about its potential role(s) during breast cancer progression. Because BSP is secreted and is present in the serum, the positivity of breast cancer cells for BSP could have been the result of an uptake of the circulating phosphoprotein by the cells rather than of an intrinsic expression. We examined the expression of BSP at both theproteinand mRNA levels in nine human breast cancer samples as well as in three human breast cancer cell lines (MCF-7, T47-D, and MDA-MB-231) using immunohistochemistry, flow cytometric analysis, immunoblot, and reverse-transcriptase PCR. BSP was detected at bothproteinand mRNA levels in human breast cancer tissue and in the three human breast cancer cell lines. Using a specific polyclonal anti-BSP antibody, we showed by both fluorescence-activated cell sorter analysis and immunohistochemistry experiments that all of the human breast cancer cell lines studied express BSP. This was localized at the cell surface and in the cytosol of the estrogen receptor-positive MCF-7 and T47-D cell lines, whereas it was detected only in the cytosol of the estrogen receptor-negative MDA-MB-231 cells. Using the same polyclonal anti-BSP antibody, we were able to identify an approximately 97-kdband on totalproteinextracts from the three cell lines by immunoblotting. Reverse-transcriptase PCR reactions using specific oligonucleotides performed on total RNA of nine human breast cancer biopsy samples and the three cell lines demonstrated the presence of BSP mRNA in all of the samples examined. This study is the first demonstration that human malignant breast epithelial cell lines express BSP at theproteinand mRNA levels. Our study identified MCF-7, T47-D, and MDA-MB-231 cells as useful models for the examination of the molecular mechanisms involved in the ectopic expression of BSP in breast malignant lesions.

## DRUG DESCRIPTORS:

\*messenger rna--endogenous compound--ec; \*sialoprotein--endogenous compound  
--ec

## MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \* breast cancer --etiology--et; \*

protein determination

antibody detection; article; cellular distribution; epithelium cell; female  
; human; human cell; human tissue; immunohistochemistry; molecular biology;  
priority journal; protein expression; protein localization

## SECTION HEADINGS:

005 General Pathology and Pathological Anatomy

22/5/14 (Item 9 from file: 72)

DIALOG(R) File 72:EMBASE

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05995868 EMBASE No: 1995024512

**Autoantibodies to 90kD heat-shock protein in sera of breast cancer  
patients (5)**

Conroy S.E.; Gibson S.L.; Brunstrom G.; Isenberg D.; Luqmani Y.; Latchman  
D.S.

Department of Molecular Pathology, Univ. College London Medical  
School, London W1P 6DP United Kingdom

Lancet ( LANCET ) (United Kingdom) 1995, 345/8942 (126)

CODEN: LANCA ISSN: 0140-6736

DOCUMENT TYPE: Journal; Letter

LANGUAGE: ENGLISH

## DRUG DESCRIPTORS:

\*autoantibody--endogenous compound--ec; \*heat shock protein

immunoglobulin g antibody--endogenous compound--ec

## MEDICAL DESCRIPTORS:

\*breast cancer --etiology--et; \* breast cancer -- diagnosis --di

antibody blood level; cancer immunology; clinical article; clinical trial;

controlled study; diagnostic test; enzyme linked immunosorbent assay;

female; human; letter; metastasis--diagnosis --di; multivariate analysis;

priority journal; prognosis; systemic lupus erythematosus--etiology--et

## SECTION HEADINGS:

005 General Pathology and Pathological Anatomy

016 Cancer

026 Immunology, Serology and Transplantation

22/5/15 (Item 10 from file: 72)

DIALOG(R) File 72:EMBASE

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05553690 EMBASE No: 1993321790

**Nova, the paraneoplastic Ri antigen, is homologous to an RNA-binding  
protein and is specifically expressed in the developing motor system**

Buckanovich R.J.; Posner J.B.; Darnell R.B.

Molecular Neuro-Oncology Laboratory, Rockefeller University, New York, NY  
10021 United States

Neuron ( NEURON ) (United States) 1993, 11/4 (657-672)

CODEN: NERNE ISSN: 0896-6273

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Paraneoplastic opsoclonus-ataxia, a disorder of motor control, develops  
in breast or lung cancer patients who harbor an antibody (Ri) that  
recognizes their tumors and a nuclear neuronal protein of 55 kd . We  
have characterized a gene, Nova, encoding an antigen recognized by the Ri  
antibody. Nova encodes a novel, highly conserved protein , homologous to  
the RNA-binding protein hnRNP K, the yeast splicing protein MER1, and a  
motif in several retroviral proteases. Northern blot analysis detects Nova

transcripts only in brain, and several alternatively spliced forms are present in brain and tumor cells. Nova expression is restricted to the ventral brain stem and spinal cord in E18 mice. Since Nova encodes a target antigen in the motor disorder paraneoplastic opsoclonus-ataxia that is expressed in the developing subcortical motor system, it is a likely participant in both the pathogenesis of paraneoplastic opsoclonus-ataxia and the developmental biology of the motor system. The homology between Nova and hnRNP K suggests that Nova regulates RNA splicing or metabolism in a specific subset of developing neurons.

DRUG DESCRIPTORS:

\*antigen; \*rna bindingprotein

MEDICAL DESCRIPTORS:

\*motor dysfunction--etiology--et; \*motor dysfunction--complication--co; \*paraneoplastic syndrome--complication--co; \*paraneoplastic syndrome--etiology--et

antigen expression; article; **breast cancer** -- diagnosis --di; development; gene expression regulation; gene location; gene structure; human; human cell; human tissue; lung cancer--**diagnosis** --di; motor system; nerve cell necrosis--etiology--et; northern blotting; priority journal; **protein** analysis; sequence homology

SECTION HEADINGS:

- 008 Neurology and Nerosurgery
- 029 Clinical and Experimental Biochemistry

22/5/16 (Item 11 from file: 72)

DIALOG(R) File 72:EMBASE

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05552762 EMBASE No: 1993320862

**Association of MMP-2 activation potential with metastatic progression in human breast cancer cell lines independent of MMP-2 production**

Azzam H.S.; Arand G.; Lippman M.E.; Thompson E.W.

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Journal of the National Cancer Institute ( J. NATL. CANCER INST. ) ( United States) 1993, 85/21 (1758-1764)

CODEN: JNCIA ISSN: 0027-8874

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Background: Expression of matrix metalloproteinase-2 (MMP-2), the 72-kd type IV collagenase/gelatinase, by cancer cells has been implicated in metastasis through cancer cell invasion of basement membranes mediated by degradation of collagen IV. However, the abundance of this latent proenzyme in normal tissues and fluids suggests that MMP-2 proenzyme utilization is limited by its physiological activation rather than expression alone. We previously reported activation of this proenzyme by normal and malignant fibroblastoid cells cultured on collagen I (vitrogen) gels. Purpose: Our purposes in this study were 1) to determine whether MMP-2 activation is restricted to the more invasive human breast cancer cell lines and 2) to localize the activating mechanism. Methods: Zymography was used to monitor MMP-2 activation through detection of latent MMP-2 (72kd) and mature species of smaller molecular weight (59 or 62kd). Human breast cancer cell lines cultured on plastic, vitrogen, and other matrices were thus screened for MMP-2 activation. Collagen I-cultured cells were exposed to cycloheximide, a protein synthesis inhibitor, or to protease inhibitors to determine the nature of the MMP-2-activating mechanism. Triton X-114 (TX-114) detergent extracts from cells cultured on collagen I or plastic were incubated with latent MMP-2 and analyzed by zymography to localize the MMP-2 activator. Results: MMP-2 activation was only induced by collagen I culture in the more aggressive, highly invasive estrogen receptor-negative, vimentin-positive human breast cancer cell lines (Hs578T, MDA-MB-436, BT549, MDA-MB-231, MDA-MB-435, MCF-7(ADR)) and was independent of MMP-2

production. MMP-2 activation was detected in cells cultured on collagen I gels but not in those cultured on gelatin gels, Matrigel, or thin layers of collagen I or IV, gelatin, or fibronectin. Collagen-induced activation was specific for the enzyme species MMP-2, since MMP-9, the 92-kD type IV collagenase/gelatinase, was not activatable under similar conditions. MMP-2 activation was inhibited by cycloheximide and was sensitive to a metalloproteinase inhibitor but not to aspartyl, serine, or cysteinyl protease inhibitors. MMP-2 activation was detected in the hydrophobic, plasma membrane-enriched, TX-114 extracts from invasive collagen I-cultured cells. Conclusion: Collagen I-induced MMP-2 activation is restricted to highly invasive estrogen receptor-negative, vimentin-positive human breast cancer cell lines, is independent of MMP-2 production, and is associated with metastatic potential. Our findings are consistent with plasma membrane localization of the activator. Implications: The MMP-2 activation mechanism may represent a new target for diagnosis, prognosis, and treatment of human breast cancer.

#### DRUG DESCRIPTORS:

\*gelatinase--endogenous compound--ec  
collagen type 1--endogenous compound--ec; collagen type 4--endogenous compound--ec; fibronectin; gelatin

#### MEDICAL DESCRIPTORS:

##### \*breast cancer

article; cancer growth; cell membrane; cellular distribution; controlled study; enzyme activation; enzyme localization; female; human; human cell; metastasis; priority journal

CAS REGISTRY NO.: 9040-48-6 (gelatinase); 86088-83-7 (fibronectin);  
9000-70-8 (gelatin)

#### SECTION HEADINGS:

016 Cancer

22/5/17 (Item 12 from file: 72)

DIALOG(R)File 72:EMBASE

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05467034 EMBASE No: 1993235133

#### Biochemistry and molecular biology of MCA

Maurer A.; Burckhardt J.

Roche Diagnostic Systems, Division of F. Hoffmann-La Roche Ltd, Basel  
Switzerland

International Journal of Biological Markers ( INT. J. BIOL. MARKERS ) ( Italy) 1993, 8/2 (108-112)

CODEN: IBMAE ISSN: 0393-6155

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The mucin-like carcinoma-associated antigen (MCA) is a mucin with a molecular weight of 350 - 500kD . It circulates in the serum and its serum content can be determined with the Cobas Core MCA EIA test. Patients with breast cancer show elevated MCA serum levels. The molecule has a polypeptide backbone consisting of three parts: the C-terminus the N-terminus and the transmembrane sequences. The protein is heavily glucosylated with carbohydrate side chains that contain fucose, galactose and N-acetyl galactosamine. The antibody b-12 recognizes a repetitive epitope on the peptide portion of the MCA molecule. The epithelial mucin, which is coded by a unique gene, was cloned using PCR technology. Peptides corresponding to the N- and C-terminus were expressed in E. coli. Analysis of the purified peptides revealed molecular weights of 12 and 18kD .

#### DRUG DESCRIPTORS:

\*monoclonal antibody; \*mucin--endogenous compound--ec; \*mucin like carcinoma associated antigen--endogenous compound--ec

#### MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \*molecular cloning

article; biochemistry; female; human; human tissue; immunochemistry

SECTION HEADINGS:

016 Cancer

026 Immunology, Serology and Transplantation

22/5/18 (Item 13 from file: 72)

DIALOG(R) File 72:EMBASE

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05421037 EMBASE No: 1993189136

**Immunocytochemical determination of pro-Cathepsin D: A significant independent prognostic indicator in early-stage breast cancer**

Gasparini G.; Bevilacqua P.; Meli S.; Bolzicco G.P.; Testolin A.; Cazzavillan S.; La Malfa G.; Marubini E.; Pozza F.

St Bortolo Regional Hospital, 36100 Vicenza Italy

Breast Disease ( BREAST DIS. ) (United States) 1993, 6/2 (85-97)

CODEN: BRDIE ISSN: 0888-6008

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Pro-Cathepsin D is a proteolytic enzyme involved in tumor invasiveness. Sections from 108 primary breast carcinomas were stained immunocytochemically by the monoclonal antibody D7 E3 against the 52-Kd protein. Overall, 29% of tumors were immunoreactive, presenting cytoplasmic labeling and positivity, for pro-Cathepsin D (pro-Cath-D) was poorly associated with cell kinetics (detected by Ki-67 monoclonal antibody), ploidy, and conventional pathologic features. The relapse-free survival (RFS) probability at 3 years was significantly worse for patients with pro-Cath-D positive tumors ( $p = 0.03$ ) as well as for patients with high proliferative tumors ( $Ki-67 > 7.5\%$ ) ( $p = 0.002$ ), axillary node involvement ( $p = 0.016$ ), and poorly differentiated tumors ( $p = 0.04$ ). Univariate analysis showed that pro-Cath-D and cell kinetics give important prognostic information concerning RFS with odds ratios of 2.50 and 3.52, respectively, as well as node status and grading (odds ratio of 2.59 and 2.19, respectively). Concerning overall survival, only node status ( $p = 0.044$ ) had prognostic significance at 3 years from surgery, but this analysis should be interpreted with caution because of the relatively short follow-up time. Combining pro-Cath-D with cell kinetics and node status made it possible to classify patients in subsets at different risk of recurrence. Multivariate statistical analysis on RFS shows that pro-Cath-D, when adjusted for nodal status cell kinetics and ploidy, is a significant and independent prognostic factor in patients with early-stage breast cancer. In conclusion, the presence of pro-Cath-D in breast cancer is associated with poor prognosis, and the determination also of Ki-67 and node status improves the capability to identify subsets of patients more likely to have recurrent and/or aggressive disease who would benefit of aggressive adjuvant therapy from those with good prognosis who need surgery alone.

DRUG DESCRIPTORS:

\*biological marker--endogenous compound--ec; \*cathepsin d--endogenous compound--ec; \*tumor marker--endogenous compound--ec  
cyclophosphamide--drug therapy--dt; fluorouracil--drug therapy--dt;  
methotrexate--drug therapy--dt; monoclonal antibody ki 67; tamoxifen--drug dose--do; tamoxifen--drug therapy--dt; unclassified drug

MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \* breast cancer --drug therapy--dt; \* breast cancer --surgery--su; \*immunocytochemistry; \*prognosis  
adult; aged; article; cancer adjuvant therapy; cancer invasion; cancer recurrence--etiology--et; cancer survival; cell kinetics; female; human; human tissue; immunoreactivity; lymph node metastasis--complication--co; major clinical study; ploidy; recurrence risk; statistical analysis  
DRUG TERMS (UNCONTROLLED): procathepsin d--endogenous compound--ec  
CAS REGISTRY NO.: 9025-26-7 (cathepsin d); 50-18-0 (cyclophosphamide);



51-21-8 (fluorouracil); 15475-56-6, 59-05-2, 7413-34-5 (methotrexate);  
10540-29-1 (tamoxifen)

## SECTION HEADINGS:

016 Cancer  
037 Drug Literature Index

22/5/19 (Item 14 from file: 72)

DIALOG(R) File 72:EMBASE

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05342847 EMBASE No: 1993110932

**Heat shockprotein hsp70 in patients with axillary lymph node-negative breast cancer: Prognostic implications**

Ciocca D.R.; Clark G.M.; Tandon A.K.; Fuqua S.A.W.; Welch W.J.; McGuire W.L.

Division of Medical Oncology, Department of Medicine, Texas Univ. Health Science Center, 7703 Floyd Curl Dr., San Antonio, TX 78284-7884 United States

Journal of the National Cancer Institute ( J. NATL. CANCER INST. ) ( United States) 1993, 85/7 (570-574)

CODEN: JNCIA ISSN: 0027-8874

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Background: Cell synthesis of heat shock (stress-response) proteins is increased by a variety of environmental and pathophysiological stressful conditions. The 70-kd heat shock protein (hsp70) is thought to be involved in protein-protein interactions including those of the protein products of the human c-myc oncogene and the p53 (also known as TP53) tumor suppressor gene. Purpose: The purpose of this study was to investigate whether elevated hsp70 expression may be an indicator of biological stress experienced by a breast cancer and may, therefore, predict disease outcome. Methods: Levels of hsp70 were determined by Western blot analysis in primary breast tumors from patients with negative axillary lymph nodes. We performed exploratory data analyses on a set of 162 primary breast cancers and constructed prognostic indexes of hsp70 expression levels. The optimal cutpoint for hsp70 expression was considered to be the value yielding the greatest separation for disease-free survival for the resulting two groups of patients. The cutpoint was then validated in a set of 345 tumors by univariate and multivariate analyses. Data were analyzed for overall survival, disease-free survival, tumor size, and patient age, as well as estrogen receptor and progesterone receptor status, ploidy (DNA content), and percentage of cells in S phase as determined by flow cytometry. Results: Expression of hsp70 emerged as a useful prognostic factor, both in univariate and in multivariate analyses. Patients whose tumors had high expression of hsp70 had significantly shorter disease-free survival ( $P = .006$ ). The other statistically significant factors were S-phase fraction ( $P = .008$ ) and tumor size ( $P = .01$ ). For patients who received adjuvant therapy, hsp70 was the only independent predictor of disease recurrence ( $P = .05$ ). For those with tumors 1-3 cm in diameter, hsp70 ( $P = .008$ ) and S-phase fraction ( $P = .02$ ) were statistically significant predictors of recurrence. Conclusions: Measurement of hsp70 expression in primary tumors from patients with node-negative breast cancer may be useful in identifying patients at high risk for disease recurrence and thus may affect decisions regarding treatment after surgery. Implications: Future studies should be performed to determine if detection of hsp70 by immunohistochemistry can be used to predict clinical outcome and to better understand the relationships between hsp70 and the effects of various treatment modalities.

## DRUG DESCRIPTORS:

\*heat shockprotein --endogenous compound--ec

## MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \* breast cancer --epidemiology--ep; \*

lymph node metastasis--**diagnosis** --di  
 article; cancer recurrence; cancer survival; cell cycle s phase; gene  
 expression; human; human tissue; major clinical study; priority journal;  
 prognosis; stress; tumor volume

## SECTION HEADINGS:

016 Cancer

22/5/20 (Item 15 from file: 72)

DIALOG(R) File 72:EMBASE

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05285746 EMBASE No: 1993053831

**Autoantibodies to a 128- kd synaptic protein in three women with the  
 stiff- man syndrome and breast cancer**

Folli F.; Solimena M.; Cofield R.; Austoni M.; Tallini G.; Fassetta G.;  
 Bates D.; Cartledge N.; Bottazzo G.F.; Piccolo G.; De Camilli P.

Department of Cell Biology, Boyer Center for Molecular Medicine, Howard  
 Hughes Medical Institute, 295 Congress Ave., New Haven, CT 06510 United  
 States

New England Journal of Medicine ( NEW ENGL. J. MED. ) (United States)

1993, 328/8 (546-551)

CODEN: NEJMA ISSN: 0028-4793

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

**Background.** The stiff-man syndrome is a rare disease of the central nervous system characterized by progressive rigidity of the body musculature. Autoantibodies directed against glutamic acid decarboxylase are present in about 60 percent of patients with the syndrome. In this group, there is a striking association of the stiff-man syndrome with organ-specific autoimmune diseases, primarily insulin-dependent diabetes mellitus. **Methods.** We studied three women with the stiff-man syndrome and breast cancer, seeking autoantibodies directed against nervous system antigens in serum and cerebrospinal fluid by immunocytochemical techniques, Western blotting, and immunoprecipitation. **Results.** Autoantibodies directed against a 128-kd brain protein were found in two of the women with the stiff-man syndrome and breast cancer. These results led to a search for breast cancer in the third patient with the stiff-man syndrome, who also had autoantibodies. A small invasive ductal carcinoma was detected by ultrasonography and removed. Serum samples from all three patients were negative for autoantibodies directed against glutamic acid decarboxylase. Autoantibodies against the 128-kd antigen were not detected in control patients with the stiff-man syndrome without breast cancer or in patients with cancer who did not have the syndrome. Within the nervous system, the 128-kd autoantigen was localized in neurons and concentrated at synapses. **Conclusions.** In a subgroup of patients with the stiff-man syndrome, the condition is likely to have an autoimmune paraneoplastic origin. The detection of autoantibodies against the 128-kd antigen in patients with this syndrome should be considered an indication to search for an occult breast cancer.

## DRUG DESCRIPTORS:

\*autoantibody

4 aminobutyric acid; glutamate decarboxylase

## MEDICAL DESCRIPTORS:

\***breast cancer** -- diagnosis --di; \* breast cancer --etiology--et; \*stiff  
 man syndrome--etiology--et; \*stiff man syndrome--**diagnosis** --di  
 adult; aged; antibody blood level; article; case report; echography; female  
 ; human; immunoblotting; immunocytochemistry; immunoprecipitation; insulin  
 dependent diabetes mellitus--epidemiology--ep; insulin dependent diabetes  
 mellitus--**diagnosis** --di; muscle rigidity; occult blood; pancreas islet  
 beta cell; priority journal

CAS REGISTRY NO.: 28805-76-7, 56-12-2 (4 aminobutyric acid); 9024-58-2 (  
 glutamate decarboxylase)

## SECTION HEADINGS:

006 Internal Medicine  
 008 Neurology and Nerosurgery  
 026 Immunology, Serology and Transplantation

22/5/21 (Item 1 from file: 73)

DIALOG(R) File 73:EMBASE

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05121590 EMBASE No: 1992261806

**Application of anti lung adenocarcinoma monoclonal antibody recognizing cytokeratin-like cytoplasmic antigen for tumordiagnosis**

Shitara K.; Fujiwara K.; Kusano A.; Yamaguchi K.; Yoshida H.; Sato S.; Hanai N.

Tokyo Research Laboratories, Kyowa Hakko Kogyo Co Ltd, Machida-shi, Tokyo 194 Japan

Anticancer Research ( ANTICANCER RES. ) (Greece) 1992, 12/4 (1121-1129)

CODEN: ANTRD ISSN: 0250-7005

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

An anti lung adenocarcinoma murine monoclonal antibody (MoAb) KM195 (IgGinf 1,) was generated using mice which underwent tolerance treatment to normal lung tissues. KM195 was selected from among a number of hybridoma clones because of its advantageous reactivity such as high binding to cell membranes of lung adenocarcinoma tissues and low binding to cell membranes of major normal tissues. In a binding assay using cultured cell lines KM195 was found to bind cytoplasmic antigen in many adenocarcinoma cells. Detailed immunohistochemical analysis using paraffin-fixed tissue sections showed that many adenocarcinoma cells such as gastric cancer colorectal cancer pancreati cancer mammary cancer ovary cancer and cervical cancer reacted positively with KM195 as well as lung adenocarcinoma cells. KM195 also positively stained a small number of normal cells found in adult and fetal tissues like lung intestine pancreatic liver and kidney. Western blot analysis using membrane fraction of lung adenocarcinoma tissues revealed two major KM195-positive bands which were electrophoresed nearby at molecular weights (M.W.) of 40Kd . The protein corresponding to the two major bands was purified by immuno-affinity chromatography and sequenced. The amino-terminal 19 residues of the lower band was identified as VLEVDPNIQAVXTQEXEQI which is identical to that of the human cytokeratin 8 (residues 77 to 95) M.W. 52Kd. The amino-terminal sequence of the upper band was blocked and not determined. To examine the ability of KM195 for tumor imaging, sup 1sup 2sup 5I-labeled KM195 was injected i.v. into nude mice bearing SW1116 xenografts. Significantly higher radioactivity was observed in the tumor compared with major organs at days 3 and 5. These data indicate that KM195, which recognizes cytokeratin 8-like cytoplasmic antigen, could be a potential MoAb for use in the immunohistochemical **diagnosis**and radioimmunodetection of adenocarcinoma.

## DRUG DESCRIPTORS:

\*carbohydrate antigen--endogenous compound--ec; \*cytokeratin--endogenous compound--ec; \*monoclonal antibody--pharmacology--pd; \*tumor antigen --endogenous compound--ec

membrane antigen--endogenous compound--ec; unclassified drug

## MEDICAL DESCRIPTORS:

\*antibody affinity; \*cell membrane; \*lung adenocarcinoma--**diagnosis** --di article;**breast cancer** -- diagnosis --di; cancer tissue-- diagnosis --di; colorectal cancer--**diagnosis** --di; xenograft; human; human cell; human tissue; immunoblotting; immunohistochemistry; molecular weight; ovary cancer--**diagnosis** --di; pancreas cancer-- diagnosis --di; priority journal ;**protein**analysis; radioimmunoassay; stomach cancer-- diagnosis --di; uterine cervix cancer--**diagnosis** --di

DRUG TERMS (UNCONTROLLED): monoclonal antibody km195--pharmacology--pd

## SECTION HEADINGS:

014 Radiology  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
016 Cancer  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index

22/5/22 (Item 2 from file: 73)

DIALOG(R) File 73:EMBASE

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04624771 EMBASE No: 1991118814

**Anti-Ri: An antibody associated with paraneoplastic opsoclonus and breast cancer**

Luque F.A.; Furneaux H.M.; Ferziger R.; Rosenblum M.K.; Wray S.H.; Schold Jr. S.C.; Glantz M.J.; Jaeckle K.A.; Biran H.; Lesser M.; Paulsen W.A.; River M.E.; Posner J.B.

1275 York Avenue, New York, NY 10021 United States

Annals of Neurology ( ANN. NEUROL. ) (United States) 1991, 29/3

(241-251)

CODEN: ANNE D ISSN: 0364-5134

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The serum and cerebrospinal fluid (CSF) of 8 women with ataxia, 6 of whom also had eye movement abnormalities believed to be opsoclonus, were found to contain a highly specific antineuronal antibody we call anti-Ri. Seven of the 8 women also had or developed cancer: carcinoma of the breast in 5, adenocarcinoma in an axillary lymph node in 1, and carcinoma of the fallopian tube in 1. Four patients presented with the neurological disorder; the cancer was diagnosed first in the other 4.

Immunohistochemical studies using serum of CSF from all 8 patients revealed a highly specific antibody interaction with central nervous system neuronal nuclei but not with glial or other cells; the titer ranged from 1:5,000 to 1:320,000 in serum and from 1:2,000 to 1:16,000 in CSF. Biotinylated IgG from the patients' serum reacted with the tumors of 3 of 4 patients with anti-Ri antibody but not with breast cancers from patients without anti-Ri antibody. Immunoblots against cerebral cortex neuronal extracts identified protein antigens of 55- kd and 80- kd relative molecular mass. Serum titers by immunoblot ranged from 1:500 to more than 1:40,000 and CSF titers, from 1:10 to 1:2,000. The relative amount of anti-Ri was always higher in CSF than in serum. The antibody was not present in sera from normal individuals; patients with breast cancer without opsoclonus; other patients with opsoclonus; or patients with other paraneoplastic syndromes related to breast, ovarian, or small-cell lung cancer. We conclude that the presence of anti-Ri antibody identifies a subset of patients with paraneoplastic ataxia and eye movement disorders (opsoclonus) who usually suffer from breast or other gynecological cancer; the antibody when present is a useful marker for an underlying malignancy.

**DRUG DESCRIPTORS:**

\*antibody--endogenous compound--ec; \*antineoplastic agent--drug therapy--dt  
cyclophosphamide--drug therapy--dt; doxorubicin--drug therapy--dt;  
fluorouracil--drug therapy--dt; prednisone--drug therapy--dt

**MEDICAL DESCRIPTORS:**

\*breast cancer ; \*opsoclonus; \*paraneoplastic syndrome-- diagnosis --di; \*  
paraneoplastic syndrome--etiology--et  
adult; aged; article; clinical article; female; human; human tissue;  
priority journal

CAS REGISTRY NO.: 50-18-0 (cyclophosphamide); 23214-92-8, 25316-40-9 (  
doxorubicin); 51-21-8 (fluorouracil); 53-03-2 (prednisone)

**SECTION HEADINGS:**

005 General Pathology and Pathological Anatomy  
008 Neurology and Neurosurgery  
016 Cancer

026 Immunology, Serology and Transplantation  
037 Drug Literature Index

22/5/23 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

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04596392 EMBASE No: 1991090435

**Characterization and histopathological correlation of cytosol proteins of benign and malignant breast tumors**

Khanna H.D.; Das D.; Kashyap J.N.; Gupta S.; Khanna S.

Department of Biophysics, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221 005 India

Journal of Surgical Oncology ( J. SURG. ONCOL. ) (United States) 1991, 46/2 (133-138)

CODEN: JSONA ISSN: 0022-4790

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Significant differences in cytosol protein level exist between normal/benign and cancerous breast tissues. There is a positive correlation between the cytosol protein level and histological grade of carcinoma. Well-differentiated carcinoma have a lower value of cytosol protein than poorly differentiated carcinoma. In slab gel electrophoregrams, the total numbers of bands are almost identical in normal, benign, and malignant conditions. In addition, 37Kd protein band is consistently present in malignant cases and always absent in normal or benign cases. More extensive biophysical examination of this band may provide further insight into the protein alterations in cancer cells at the molecular level.

**DRUG DESCRIPTORS:**

\*cytosine; \*protein

**MEDICAL DESCRIPTORS:**

\*breast cancer -- diagnosis --di

adult; article; clinical article; female; histopathology; human; human tissue; priority journal

CAS REGISTRY NO.: 71-30-7 (cytosine); 67254-75-5 (protein )

**SECTION HEADINGS:**

005 General Pathology and Pathological Anatomy

009 Surgery

016 Cancer

22/5/24 (Item 4 from file: 73)

DIALOG(R) File 73:EMBASE

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04558962 EMBASE No: 1991053005

**Plasmin receptors on breast tumor cells. Relation with invasiveness**

Correc P.; Fondaneche M.C.; Burtin P.

IRSC/CNRS UPR 277, BP 8, 94801 Villejuif Cedex France

Bulletin du Cancer ( BULL. CANCER ) (France) 1990, 77/SUPPL. 1 (193s-197s)

CODEN: BUCAB ISSN: 0007-4551

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH

We studied the plasmin receptor on three MCF-7 variants: MCF7, MCF7R which was derived by transfection with v-Ha-ras oncogene and MCF7MF which was studied for secretion of procathepsin D in the presence of estrogen. All three variants bound plasmin with a higher affinity than plasminogen. In each case, the number of binding sites was increased about 4-fold by a weak proteolytic pretreatment of cells. Transfection by v-Ha-ras oncogene apparently did not change the affinity of plasmin binding sites (Kd= 27

nM against 26 nM for MCF7) and increased their number very slightly (3,200 against 3,800 fmoles/mgprotein ). However, this number was 5-fold higher for MCF7MF. This is the only variant to be invasive in an in vitro invasion assay system.

DRUG DESCRIPTORS:

\*plasmin

MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \*cancer infiltration

conference paper; female; human; human tissue; priority journal

CAS REGISTRY NO.: 9001-90-5, 9004-09-5 (plasmin)

SECTION HEADINGS:

010 Obstetrics and Gynecology

016 Cancer

029 Clinical and Experimental Biochemistry

22/5/25 (Item 5 from file: 73)

DIALOG(R) File 73:EMBASE

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04530811 EMBASE No: 1991024853

**Ultrastructural localization of mRNA encoding for the EGF receptor in human breast cell cancer line BT20 by in situ hybridization**

Le Guellec D.; Frappart L.; Desprez P.Y.

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Journal of Histochemistry and Cytochemistry ( J. HISTOCHEM. CYTOCHEM. ) ( United States) 1991, 39/1 (1-6)

CODEN: JHCYA ISSN: 0022-1554

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The EGF receptor (EGF-R), a 170KDtransmembrane glycoprotein, is found at a high level in the BT20 human mammary carcinoma cell line (1 +/- 0.4 x 10sup 6 sites per cell). In this study, we examined the expression of the EGF-R gene in BT20 cell line by in situ hybridization at the light and electron microscopic level using a human cDNA, corresponding to EGF-R transmembrane andprotein kinase domains, labeled with (sup 3H)-, (sup 3sup 5S)-, or (sup 3sup 2P)-d-ATP. Two treatments were tested to embed cells in Lowicryl resin: the first used fixation and dehydration by progressive lowering of temperature, the second quick freezing and cryosubstitution. The best ultrastructural preservation was obtained with the second procedure without modification of the hybridization signal. EGF-R mRNA was observed principally at the cytoplasmic level, on organelles involved in theprotein synthesis process. Labeling was also located on the microvilli which extend into the intercellular space, suggesting that some mRNA would be located in sites where EGF-R is utilized. Some mRNA was observed in the nucleus. This study demonstrates that post-embedding in situ hybridization, after quick freezing and cryosubstitution, is a powerful EM in situ hybridization procedure to study the expression of the EGF-R gene.

DRUG DESCRIPTORS:

\*cell receptor; \*epidermal growth factor

messenger rna

MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \*cancer cell culture

article; electron microscopy; female; human; human cell; in situ

hybridization; priority journal

CAS REGISTRY NO.: 62229-50-9 (epidermal growth factor)

SECTION HEADINGS:

005 General Pathology and Pathological Anatomy

016 Cancer

22/5/26 (Item 6 from file: 73)  
DIALOG(R) File 73:EMBASE  
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03803187 EMBASE No: 1988252627

**Epithelial membrane antigen (EMA) distribution in various biological fluids**

Hendrick J.C.; Collette J.; Claes S.; Franchimont P.  
Radioimmunoassay Laboratory, Institute of Pathology, B-4000 Liege 1  
Belgium  
European Journal of Cancer and Clinical Oncology ( EUR. J. CANCER CLIN.  
ONCOL. ) (United Kingdom) 1988, 24/10 (1589-1594)  
CODEN: EJCAA ISSN: 0277-5379  
DOCUMENT TYPE: Journal  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Different human biological fluids, namely breast cyst fluids (five), milks (four), sera (five), were submitted to molecular sieving chromatography on Sepharose CL6B. Global **protein** contents of the eluted fractions were estimated by the Bradford method. Epithelial membrane antigen (EMA) was assayed by two different ELISA techniques using polyclonal and monoclonal antibodies. Various molecular species reacting with EMA (15) were found in the chromatographies with molecular weights ranging from 35 to 1500kd . But the total amount of antigens detected using polyclonal or monoclonal antibodies was quite similar. Moreover no significant difference was found between the sera from two lactating women and the sera from three women with adenocarcinoma with respect to the molecular distribution of different molecular species of EMA.

DRUG DESCRIPTORS:

\*membrane antigen

MEDICAL DESCRIPTORS:

\*breast cancer -- diagnosis --di; \*epithelium cell; \*lung cancer--  
diagnosis --di

chromatography; human cell; human

SECTION HEADINGS:

- 005 General Pathology and Pathological Anatomy
- 016 Cancer
- 029 Clinical and Experimental Biochemistry
- 026 Immunology, Serology and Transplantation

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